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=> fil hcaplus
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FILE COVERS 1907 - 1 May 2006  VOL 144 ISS 19
FILE LAST UPDATED: 30 Apr 2006  (20060430/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que l29
L1               STR
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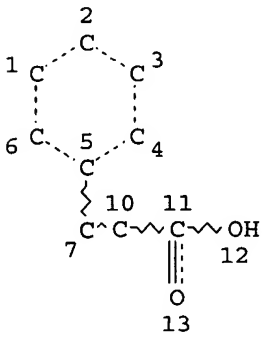


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   5
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
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L3               STR
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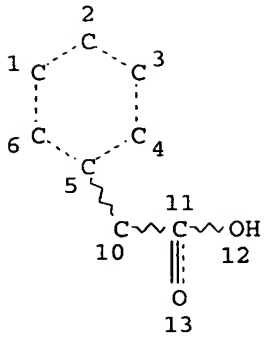

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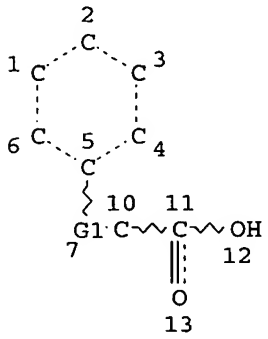
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 5
NUMBER OF NODES IS 10

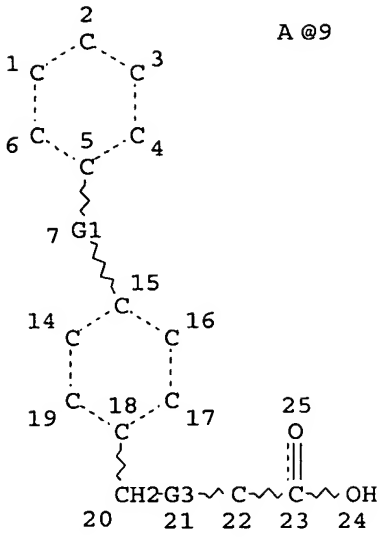
STEREO ATTRIBUTES: NONE
L4 STR



VAR G1=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 5
NUMBER OF NODES IS 11

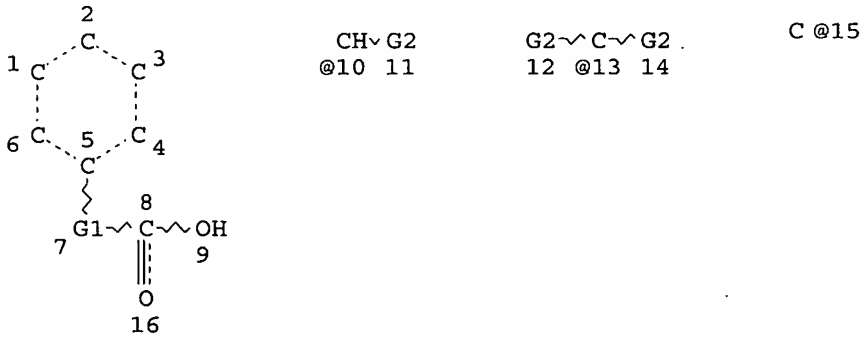
STEREO ATTRIBUTES: NONE
L5 STR



REP G1=(0-1) 9
VAR G3=O/S/N
NODE ATTRIBUTES:
NSPEC IS RC AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 14 5
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L6 105668 SEA FILE=REGISTRY SSS FUL L3 OR L4 OR L5
L14 204237 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DIABETES MELLITUS"/CV OR DIABETES/CV) OR "ANTIDIABETIC AGENTS"/CV OR HYPERGLYCEMIA/CV OR ?DIABET? OR ?HYPERGLYCEM? OR (BLD OR BLOOD)(2A)(SUGAR OR GLUCOSE) OR MUSCULAR DYSTROPHY/CV OR DYSTROPHY/CV OR MYODYSTROPHY/CV OR ?DYSTROPHY? OR ?SCLEROS?(2A)SYSTEM?
L19 STR

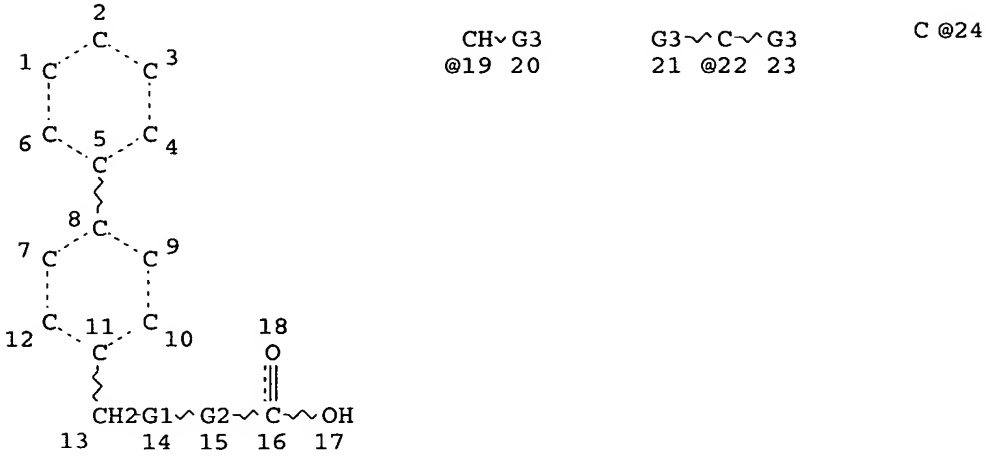


VAR G1=CH2/10/13/15
VAR G2=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 15
DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

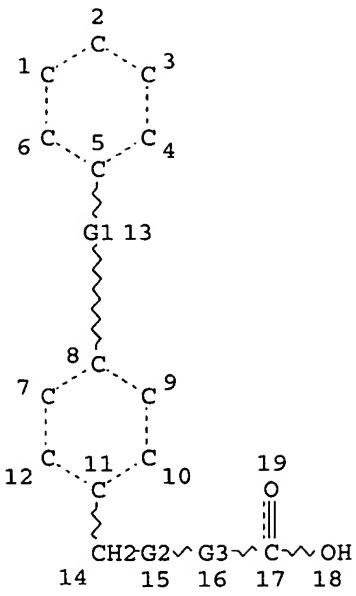
STEREO ATTRIBUTES: NONE
L20 STR



VAR G1=O/S/NH/SO2
VAR G2=CH2/19/22/24
VAR G3=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L21 STR



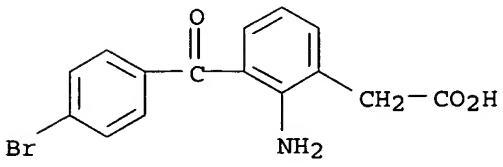

```
VAR G1=O/S/SO2/CH2/20/23/25
VAR G2=O/S/NH/SO2
VAR G3=CH2/20/23/25
VAR G4=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC   IS R      AT  25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  25

STEREO ATTRIBUTES: NONE
L22      288559 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L6
L24       27972 SEA FILE=REGISTRY SUB=L22 SSS FUL L19 OR L20 OR L21
L25       58477 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24
L26         283 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14(L)L25
L27         114 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND PD=<MAY 28, 1999
L28        7507 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25(L)(?MEDIC? OR ?THERAP? OR
                ?DRUG? OR ?PHARMA?)
L29          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 AND L28


=>
=>

=> d ibib abs hitstr l29 1-16
```

L29 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:536452 HCAPLUS
DOCUMENT NUMBER: 127:185342
TITLE: The influence of bromfenac on the pharmacokinetics and pharmacodynamic responses to glyburide in diabetic subjects
AUTHOR(S): Boni, Joseph P.; Cevallos, William H.; Decleene, Sheryl; Korth-Bradley, Joan M.
CORPORATE SOURCE: Department of Pharmacokinetics, Wyeth-Ayerst Research, Philadelphia, PA, USA
SOURCE: Pharmacotherapy (**1997**), 17(4), 783-790
CODEN: PHPYDQ; ISSN: 0277-0008
PUBLISHER: Pharmacotherapy Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To assess the effect of bromfenac sodium, a nonnarcotic analgesic drug under development, on the pharmacokinetics and pharmacodynamics of glyburide in patients with type II diabetes. Randomized, double-blind, placebo-controlled, multiple-dose study with a two-period crossover design. Eleven men and one woman (age 36-64 yrs) whose diabetes was responsive to oral sulfonylurea therapy. Placebo or bromfenac 50 mg was given as a single oral dose 3 times/day for the first 3 days of the study. On days 4-6, patients received the alternative treatment. For at least 3 mo before and during the study, patients took their usual single daily dose of glyburide 10 mg. Bromfenac concns. were measured by high-performance liquid chromatog. with UV detection. Glyburide concns. were measured by gas chromatog. with nitrogen-phosphorus detection. Glycemia was measured repeatedly on day 3 of each treatment. Pharmacokinetic anal. was performed with noncompartmental techniques. No significant differences in the pharmacokinetics of glyburide or in the pharmacodynamic response of serum glucose levels were observed between placebo and bromfenac. Intersubject variability of concns. was modest for glyburide and glucose, with a CV of 43% or less. Glyburide levels are not changed during concomitant administration of bromfenac.

IT **91714-94-2**, Bromfenac
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(influence of bromfenac on the **pharmacokinetics** and **pharmacodynamic** responses to glyburide in **diabetic** humans)

RN 91714-94-2 HCAPLUS
CN Benzeneacetic acid, 2-amino-3-(4-bromobenzoyl)- (9CI) (CA INDEX NAME)



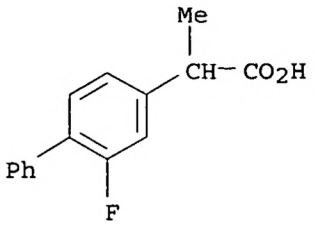
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:375709 HCAPLUS
DOCUMENT NUMBER: 125:48726
TITLE: Type II collagen-induced arthritis in the diabetic-resistant BioBreeding rat: inflammatory and histopathological features of joint pathology and effects of antiinflammatory and antirheumatic drugs on this chronic arthritic process
AUTHOR(S): Smith, Robert J.; Sly, Laurel M.
CORPORATE SOURCE: Dep. Cell Biol. Inflammation Res., Pharmacia & Upjohn, Inc., Kalamazoo, MI, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1996**), 277(3), 1801-1813
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diabetic-resistant (DR) BioBreeding (BB) rats developed an erosive hind paw arthritis when immunized with an emulsion of bovine type II collagen (CII) and incomplete Freund's adjuvant. Macroscopic clin. evidence of type II collagen-induced arthritis (CIA) first appeared as periarticular erythema and edema in the hind paws between days 9 and 10 post-immunization with CII. The incidence of CIA was 100% by day 11 in the CII-challenged rats; and CIA severity progressed over a 28-day period with radiog. evaluation revealing focal resorption of bone together with osteophyte formation in the tibiotarsal joint and soft tissue swelling; the histopathol. of CIA included an hyperplastic synovium that invaded and eroded articular cartilage at the joint margins, and subchondral bone resorption associated with bone-derived, multinucleated cell-containing granulomatous lesions in the rat hind paw. The corticosteroid, methylprednisolone (medrol), and the nonsteroidal antiinflammatory drug, flurbiprofen (Ansaid), administered at 2 mg/kg (p.o.), suppressed the clin. signs of CIA, and caused 79 to 83% inhibition of hind paw inflammation. However, methylprednisolone, but not flurbiprofen, inhibited the joint pathol. in CIA. The antirheumatic drugs, cyclophosphamide (cytoxan, 5 mg/kg, p.o.) and cyclosporin A (CsA, 25 mg/kg, p.o.) suppressed the cartilage erosion in inflamed rat joints, and exerted marked inhibition (89-100%) of hind paw swelling. Methotrexate (0.15 mg/kg, p.o.) treatment reduced hind paw swelling (48%), whereas azathioprine, D-penicillamine (DP) and the oral gold preparation, auranofin, were inactive. Anti-CII antibody titers were completely suppressed by cyclosporin A and cytoxan. Radiog. evidence of protection from bone resorption, osteophyte formation and soft tissue swelling was apparent in the tibiotarsal joints of cytoxan, cyclosporin A, methylprednisolone and methotrexate-treated rat.

IT **5104-49-4**, Flurbiprofen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type II collagen-induced arthritis in the **diabetic**-resistant BioBreeding rat: histopathol. features of joint pathol. and effects of antiinflammatory and antirheumatic **drugs**)

RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)

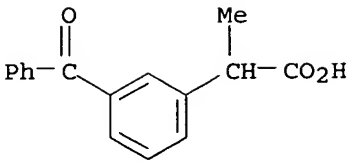

Me
CH
CO2H
Ph
F

L29 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:197935 HCAPLUS
DOCUMENT NUMBER: 124:277995
TITLE: Influence of non-steroidal anti-inflammatory drugs on the binding kinetics of dansylsarcosine to human serum albumin: stereoselectivity, steric and inductive effects
AUTHOR(S): Keita, Yango; Woerner, Wolfgang; Veile, Guido; Woodcock, Barry G.; Fuhr, Uwe
CORPORATE SOURCE: Dep. Clinical Pharmacology, Johann Wolfgang Goethe Univ., Frankfurt/Main, D-60590, Germany
SOURCE: Arzneimittel-Forschung (**1996**), 46(2), 164-8
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of a series of non-steroidal anti-inflammatory **drugs** (NSAIDs) on the binding kinetics of dansylsarcosine (CAS 72517-44-3, DS), a marker ligand for the benzodiazepine binding site, and human serum albumin (HSA) was studied using the stopped-flow method. Both native (7% glycated) and 25% glycated HSA were used. The binding parameters were determined on the basis of the consecutive model. The DS association rate constant (k2) was 649 s-1 and 375 s-1 for 7% and 25% glycated HSA, resp. These values were substantially influenced by addition of NSAIDs (molar ratio HSA:NSAID = 2:1), depending on the structure of NSAIDs. The calculated DS dissociation rate constant (k-2) was approx. 20 s-1. This value did not show marked dependence on the degree of glycation or on the presence of NSAIDs at the concentration used. The values were similar to ests. of kd (the displacement rate constant of DS) with the exception of diclofenac (CAS **15307-86-5**) where kd was significantly lower, reaching 4.8 s-1 and 4.8 s-1 vs. k-2 parameters of 14 s-1 and 15 s-1 for 7% and 25% glycated HSA, resp. A comparison of the enantiomers R- and S-ibuprofen (CAS **15687-27-1**) and the regioisomers fenbufen (CAS 36330-85-5) and ketoprofen (CAS **22071-15-4**) showed slight or no stereoselectivity of effects on the DS binding kinetics. However, the binding was influenced by bulk and nature of substituents at the aryl rest of propionic acid. The results obtained for mefenamic acid (CAS 61-68-7) suggest that this NSAID binds to a site of human serum albumin other than site II. Increased concns. of glycoalbumin, as observed in **diabetic** patients, are not presumed to have inhibitory effects addnl. to that of NSAIDs which interact differentially with **drugs** at site II of HSA.

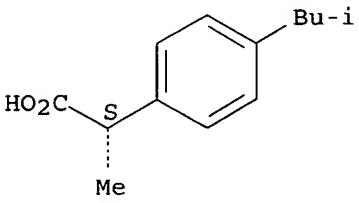
IT **22071-15-4**, Ketoprofen **51146-56-6**, S-Ibuprofen **51146-57-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structure-activity of influence of non-steroidal anti-inflammatory **drugs** on the binding kinetics of dansylsarcosine to human serum albumin)

RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



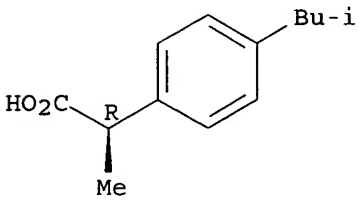
RN 51146-56-6 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 51146-57-7 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)-, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

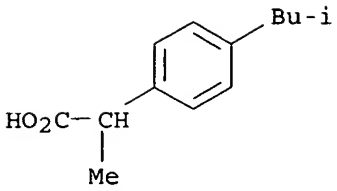


L29 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:828020 HCAPLUS
DOCUMENT NUMBER: 123:275126
TITLE: Enantioselective effects of experimental diabetes mellitus on the metabolism of ibuprofen
AUTHOR(S): Xiaotao, Qian; Hall, Stephen D.
CORPORATE SOURCE: Dep. Med., Indiana Univ. Sch. Med., Indianapolis, IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (**1995**), 274(3), 1192-8
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diabetes mellitus is associated with numerous metabolic events that may influence the elimination of R- and S-ibuprofen and the inversion of R-ibuprofen. Short (3 days) and long (14 days) term exptl. type I diabetes was induced in male Sprague-Dawley rats with streptozotocin, and genetically diabetic male Zucker rats were used as a model of type II diabetes. Isolated hepatocytes from long-term streptozotocin-treated rats exhibited significantly greater rate consts. for ibuprofenyl-CoA (CoA) formation (1.44 ± 0.05 vs. 0.60 ± 0.09 h-1) and the elimination of R-ibuprofen (0.34 ± 0.07 vs. 0.22 ± 0.07 h-1) relative to control ($P \leq .05$). These increases were consistent with significant induction of hepatic cytochrome P 450 (1.14 ± 0.45 vs. 0.54 ± 0.10 nmol/mg protein) and an elevated hepatic free CoA content (313.4 ± 48.5 vs. 172.9 ± 38.6 nmol/g) relative to control ($P \leq .05$). In hepatocytes from type II diabetic rats there were significant redns. ($P \leq .05$) in the rate consts. for ibuprofenyl-CoA formation (1.02 ± 0.12 vs. 1.22 ± 0.12 h-1), R-ibuprofen elimination (0.21 ± 0.06 vs. 0.34 ± 0.10 h-1) and S-ibuprofen elimination (0.41 ± 0.07 vs. 0.73 ± 0.11 h-1) but no change in hepatic content of cytochrome P 450 or CoA relative to control. The activity of ibuprofenyl-CoA synthetase in whole liver homogenate supplemented with ATP and CoA was not influenced by exptl. diabetes. In both type I and type II diabetes there was a significantly greater exposure of hepatocytes to ibuprofenyl-CoA. The fractional inversion of the R-enantiomer to S-ibuprofen, which is primarily responsible for the inhibition of cyclooxygenase activity that occurs in vivo, was also significantly greater ($P \leq .05$) in both type I (0.71 ± 0.11 vs. 0.59 ± 0.07) and type II (0.86 ± 0.09 vs. 0.71 ± 0.04) models of diabetes relative to controls. Diabetic patients may therefore be at greater risk from the adverse effects of increased exposure to CoA thioesters and the pharmacol. active S-ibuprofen.

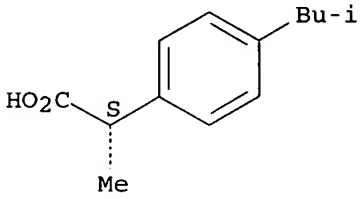
IT **15687-27-1**, Ibuprofen **51146-56-6**, S-Ibuprofen **51146-57-7**
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(enantioselective effects of **diabetes** mellitus on **pharmacokinetics** of ibuprofen)

RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



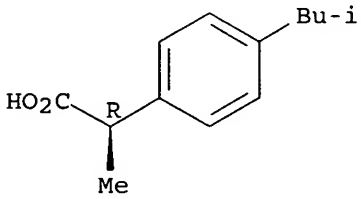
RN 51146-56-6 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 51146-57-7 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)-, (αR)- (9CI) (CA INDEX NAME)

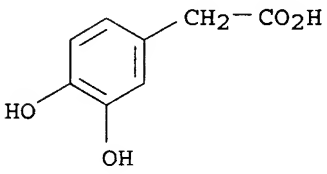
Absolute stereochemistry. Rotation (-).



L29 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:747798 HCAPLUS
DOCUMENT NUMBER: 123:195745
TITLE: Long-term experimentally-induced diabetes and catecholamine metabolism in rat brain regions
AUTHOR(S): Martin, F. J.; Miguez, J. M.; Aldegunde, M.
CORPORATE SOURCE: Dep. de Fisioloxia, Univ. Santiago Compostela, Santiago, Spain
SOURCE: Biogenic Amines (**1995**), 11(4), 305-11
CODEN: BIAME7; ISSN: 0168-8561
PUBLISHER: VSP
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tissue concns. of dopamine (DA), their major metabolite 3,4-dihydroxyphenylacetic acid (DOPAC) and noradrenaline (NA) were measured by HPLC with electrochem. detection in brain areas (corpus striatum, cortex, hippocampus, hypothalamus, medulla pons, midbrain and amygdala) and cerebellum of diabetic rats (streptozotocin-induced). Diabetic rats showed a statistically significant reduction of striatal DA and DOPAC levels and an increment of cerebellum and cortex DA content. Noradrenaline levels also increased in cerebellum and striatum. No changes were found in other brain regions. Only striatal NA and DA levels returned to control values after insulin replacement therapy. Data indicates that DA metabolism in regions with high and low DA contents are differentially affected in diabetes since different neuronal processes are altered in each dopamine brain area.

IT **102-32-9**, 3,4-Dihydroxyphenylacetic acid
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(catecholamine response in brain to streptozotocin-induced **diabetes** and insulin replacement **therapy**)
RN 102-32-9 HCAPLUS
CN Benzeneacetic acid, 3,4-dihydroxy- (9CI) (CA INDEX NAME)



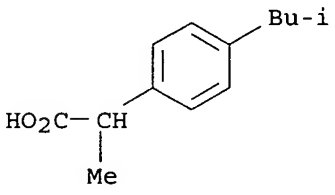
L29 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:490814 HCAPLUS
DOCUMENT NUMBER: 105:90814
TITLE: Drug interactions of EB-382, a nonsteroidal anti-inflammatory agent
AUTHOR(S): Fujiyoshi, Toshio; Iida, Hiroyuki; Yamaura, Tetsuaki; Hosono, Masahiro; Maeda, Etsuko; Saito, Masumi; Ikeda, Kenro; Uematsu, Toshio
CORPORATE SOURCE: Res. Lab., Fujirebio Inc., Hachioji, 192, Japan
SOURCE: Yakuri to Chiryo (1973-2000) (**1986**), 14(4), 2235-40
CODEN: YACHDS; ISSN: 0386-3603
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The **drug** interactions of EB-382 (alminoprofen) [**39718-89-3**] with an anticoagulant, an **antidiabetic**, and aspirin [50-78-2] were examined, and the following results were obtained. A dose-dependent potentiation of anticoagulant activity was observed after a combination of EB-382 (10 .apprx.50 mg/kg p.o.) and Warfarin [81-81-2] (1 mg/kg p.o) in rats. A dose-dependent, but not significant, potentiation of hypoglycemic activity was observed after a combination of EB-382 (50, 100 mg/kg p.o.) and tolbutamide [64-77-7] (50 mg/kg p.o.) in rats. An additive synergistic inhibition on acetic acid-induced mouse writhing response or carrageenin-induced rate hind-paw edema was observed after a combination of EB-382 (10.apprx.100 mg/kg p.o.) and aspirin (100, 300 mg/kg p.o.) or EB-382 (2, 10 mg/kg p.o.) and aspirin (100 mg/kg p.o.). Synergistic ulcerogenic activity in the rat gastric corpus was observed after a combination of EB-382 (200 mg/kg p.o.) and aspirin (300 mg/kg p.o.). However, greatly decreased ulcerogenic activity on other gastrointestinal organs was observed after combination of EB-382 and aspirin. Concurrent **therapy** with EB-382 and other **drugs**, such as anticoagulants, **antidiabetic** agents, and aspirin should be avoided.

L29 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:161703 HCAPLUS
DOCUMENT NUMBER: 104:161703
TITLE: Efficacy of some nonsteroidal antiinflammatory agents in experimental diabetes mellitus
AUTHOR(S): Nasyrov, Kh. M.; Morugova, T. V.
CORPORATE SOURCE: Bash. Med. Inst., Ufa, USSR
SOURCE: Farmakologiya i Toksikologiya (Moscow) (**1986**), 49(2), 75-8
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB The effects of the nonsteroidal antiinflammatory agents amidopyrine [58-15-1], acetylsalicylic acid [50-78-2], brufen [**15687-27-1**], and butadione [50-33-9], and of methyluracil [27942-00-3] and ascorbic acid [50-81-7] on **blood glucose**, insulin [9004-10-8], and somatotropin [9002-72-6] were studied in intact and **diabetic** rats with and without exptl. inflammation. In intact rats, amidopyrine and acetylsalicylate decreased **blood glucose** and increased insulin; brufen and ascorbate increased **blood sugar** but did not affect insulin; methyluracil increased both glucose and insulin; butadione affected neither. Growth hormone levels were decreased by acetylsalicylate and butadione and were increased by methyluracil. In intact rats with exptl. inflammation, acetylsalicylate and butadione increased blood insulin levels. Inflammation alone altered insulin (increase) and sugar (decrease) on the 3rd day after its induction. In rats with alloxan **diabetes**, all of the inflammation inhibitors increased insulin and decreased sugar. Methyluracil increased both insulin and **blood sugar** levels in **diabetic** rats. In **diabetic** rats with exptl. inflammation only butadione had no **therapeutic** effect, whereas methyluracil potentiated the antiinflammatory effects of acetylsalicylate and amidopyrine. Thus, amidopyrine, brufen, and methyluracil in addition to acetylsalicylate can be used to treat inflammation.

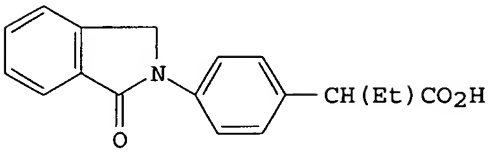
IT **15687-27-1**
RL: BIOL (Biological study)
(**blood sugar** and insulin in response to, in **diabetes**)
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L29 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:72698 HCAPLUS
DOCUMENT NUMBER: 102:72698
TITLE: Interaction between tolbutamide and certain antirheumatic agents on lipid metabolism of rats
AUTHOR(S): Ismail, Nabila A.; Shaheen, Amira A.
CORPORATE SOURCE: Fac. Pharm., Cairo Univ., Cairo, Egypt
SOURCE: Egyptian Journal of Pharmaceutical Sciences (**1984**), Volume Date 1982, 23(1-4), 233-45
CODEN: EJPSBZ; ISSN: 0301-5068
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hepatic metabolism of lipids and phospholipids was determined in adjuvant arthritic rats receiving no treatment, treatment with the nonsteroidal antiinflammatory agents phenylbutazone [50-33-9] or diclofenac Na [**15307-79-6**], treatment with the oral **antidiabetic** tolbutamide [64-77-7], or treatment with combinations of antiinflammatory agent and **antidiabetic.** Acute effects of the **drugs** were determined, as well as those after 7, 14, and 21 consecutive days of treatment. Results are given for liver cholesterol [57-88-5], cholesterol esters, triglycerides, nonesterified fatty acids, phospholipids, and total lipids, but no general pattern or conclusion is reported.

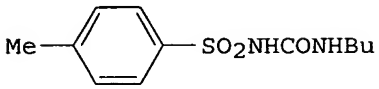
L29 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:55661 HCAPLUS
DOCUMENT NUMBER: 102:55661
TITLE: Indobufen interacts with the sulfonylurea, glipizide, but not with the β-adrenergic receptor antagonists, propranolol and atenolol
AUTHOR(S): Elvander-Staahl, Elisabeth; Melander, A.; Waahlin-Boll, Elisabeth
CORPORATE SOURCE: Health Sci. Cent., Lund Univ., Dalby, S-240 10, Swed.
SOURCE: British Journal of Clinical Pharmacology (**1984**), 18(5), 773-8
CODEN: BCPHBM; ISSN: 0306-5251
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The possible interactions of the cyclooxygenase inhibitor indobufen (I) [**63610-08-2**] with 1 sulfonylurea, glipizide [29094-61-9], and with 2 β-adrenoceptor antagonists, 1 of which is extensively metabolized already in the 1st passage through the liver (propranolol [525-66-6]) while the other essentially escapes biotransformation (atenolol [29122-68-7]), was determined Indobufen was 1st given as a single 200 mg dose and then for a 5 day period in a dosage of 200 mg, twice daily, to 6 healthy volunteers. Glipizide (5 mg), propranolol (80 mg) and atenolol (100 mg) were given as single doses before and during indobufen **medication.** The **drug** concns. were measured by selective and sensitive HPLC methods. Apparently, the lipophilic acid indobufen can inhibit the metabolic inactivation of another lipophilic acid, glipizide, but does not interfere with the disposal of the 2 basic **drugs**, propranolol and atenolol. The increased glipizide concns. following indobufen were associated with an enhanced **blood glucose** reduction Hence, this interaction may be clin. relevant.

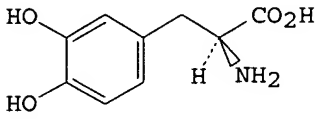
L29 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:515585 HCAPLUS
DOCUMENT NUMBER: 99:115585
TITLE: Influence of nonsteroidal anti-inflammatory agents on tolbutamide hypoglycemia
AUTHOR(S): Diwan, Prakash V.; Kulkarni, Dhruvaraj R.
CORPORATE SOURCE: Dep. Pharmacol., J.N. Med. Coll., Belgaum, India
SOURCE: Indian Journal of Medical Research (1913-1988) (**1983**), 78(July), 147-50
CODEN: IJMRAQ; ISSN: 0019-5340
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB **Drug** interaction between tolbutamide (I) [64-77-7] and commonly used nonsteroidal anti-inflammatory agents was investigated in rabbits and healthy humans. Tolbutamide lowered the **blood sugar** levels by 22-23% from the fasting value, in both rabbits and human volunteers. None of the anti-nflammatory agents altered the **blood sugar** level. However, when administered before tolbutamide, indomethacin [53-86-1], ibuprofen [**15687-27-1**], and N-β-phenethylanthranilic acid [23049-93-6] antagonized tobultamide hypoglycemia while phenylbutazone [50-33-9] did not modify the latter. The relevance of such interactions in the **therapy** of **diabetics** in clin. practice is discussed.

L29 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:400825 HCAPLUS
DOCUMENT NUMBER: 99:825
TITLE: Decreased brain dopamine synthesis rate and increased [3H]spiroperidol binding in streptozotocin-diabetic rats
AUTHOR(S): Trulson, M. E.; Himmel, C. D.
CORPORATE SOURCE: Lab. Neurobiol., Univ. Texas, Richardson, TX, USA
SOURCE: Journal of Neurochemistry (**1983**), 40(5), 1456-9
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

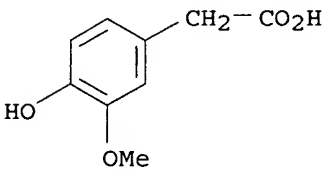


I

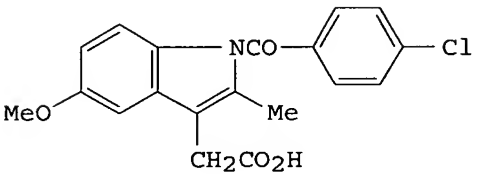
AB The rate of accumulation of dopa (I) [59-92-7] following decarboxylase inhibition and of homovanillic acid [**306-08-1**] following probenecid treatment were significantly decreased in streptozotocin-**diabetic** rats. These changes were observed in both the striatum and limbic forebrain. The Bmax for [3H]spiroperidol receptor binding was significantly increased in both brain regions. All of these neurochem. changes were reversed by insulin [9004-10-8] replacement **therapy**. Thus, **diabetes** results in a reduction in the dopamine [51-61-6] synthesis rate and an increase in [3H]spiroperidol binding in both the nigrostriatal and mesolimbic dopamine systems.

IT **306-08-1**
RL: FORM (Formation, nonpreparative)
(formation of, by brain in **diabetes**, insulin effect on)

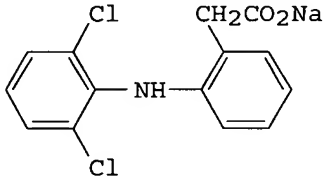
RN 306-08-1 HCAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy- (9CI) (CA INDEX NAME)



L29 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:210730 HCAPLUS
DOCUMENT NUMBER: 96:210730
TITLE: Effect of indomethacin and voltaren on carbohydrate metabolism
AUTHOR(S): Livshits, I. B.; Mrochek, A. G.; Gorbachev, V. V.; Romanchak, M. N.
CORPORATE SOURCE: USSR
SOURCE: Deposited Doc. (**1981**), VINITI 1288-81, 13 pp. Avail.: VINITI
DOCUMENT TYPE: Report
LANGUAGE: Russian
GI



I



II

AB indomethacin (I) [53-86-1] at 3 mg/kg/day for 2 days retarded the glycemic curve response in an oral glucose [50-99-7] tolerance test in rabbits; at the same dose for 60 days, I induced an increase in the glycemic curve, followed by a slow decrease. voltaren (II) [**15307-79-6**] at 3 ng/kg/day for 2 days had no effect on the oral glucose tolerance test; after 60 days of II administration, **blood glucose** levels were depressed at all stages of the oral glucose tolerance test. I at 3 ng/kg/day for 17 days had no effect on the glucose tolerance test in which glucose was administered i.v. Apparently, the actions of the 2 **drugs** tested may be due to the blockade of prostaglandin synthesis, which can alter pancreatic insulin secretion, as well as gastrointestinal glucose absorption.

L29 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:129806 HCAPLUS
DOCUMENT NUMBER: 96:129806
TITLE: Use of an analgesic and nonhormonal, antiinflammatory agent in the treatment of microvascular diseases
INVENTOR(S): Ringold, Howard J.; Waterbury, L. David
PATENT ASSIGNEE(S): Syntex Corp. , USA
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

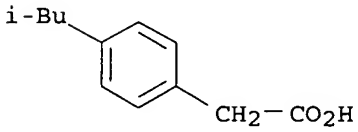
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3026402	A1	19820204	DE 1980-3026402	19800711 <--
JP 57032218	A2	19820220	JP 1980-103214	19800729 <--

PRIORITY APPLN. INFO.: DE 1980-3026402 A 19800711

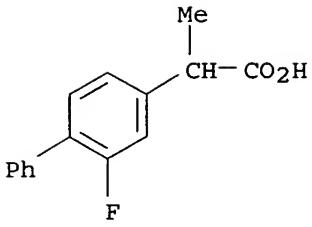
AB The microvascular diseases of man and mammals, especially of the skin, kidney, and retina, as a result of the complications of **diabetes** mellitus, are treated with a nonhormonal antiinflammatory analgesic. Thus, rats made **diabetic** with streptozotocin were fed a lab chow diet, or the diet containing 0.05% ibuprofen [**15687-27-1**] (50 mg/kg/day) or 0.015% naproxen [22204-53-1] (15 mg/kg/day) for 3 wk, and fluorescein was injected. One hour later, the penetration of fluorescein into the vitreous humor was measured. Both **drugs** reduced the penetration to normal levels, as compared to more than twice normal values in untreated **diabetic** rats. Preparation of tablets containing these ingredients is described.

IT **1553-60-2 5104-49-4 15307-79-6**
15307-86-5 15687-27-1 22071-15-4
22131-79-9 29679-58-1 31793-07-4
31842-01-0 34645-84-6 40828-46-4
51022-75-4 51579-82-9
RL: BIOL (Biological study)
(**diabetic** angiopathy treatment with)

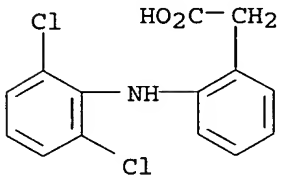
RN 1553-60-2 HCAPLUS
CN Benzeneacetic acid, 4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



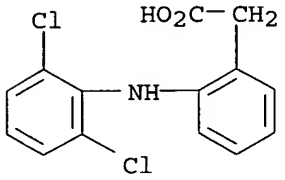
RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)



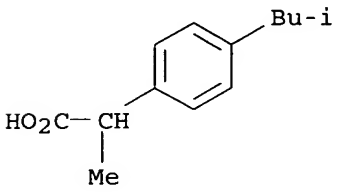
RN 15307-79-6 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)



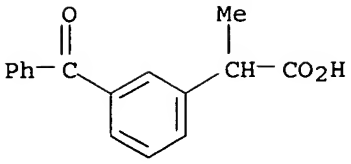
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



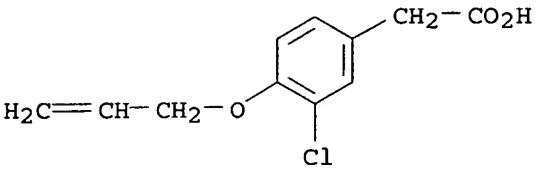
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



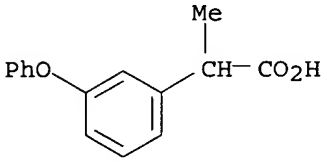
RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



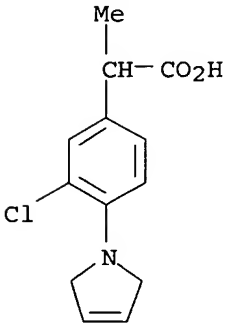
RN 22131-79-9 HCAPLUS
CN Benzeneacetic acid, 3-chloro-4-(2-propenyloxy)- (9CI) (CA INDEX NAME)



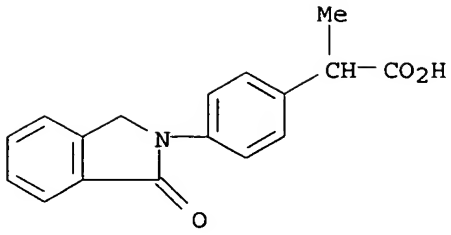
RN 29679-58-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-3-phenoxy- (9CI) (CA INDEX NAME)



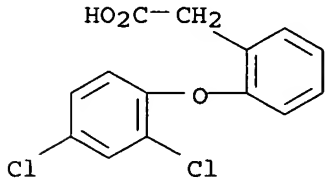
RN 31793-07-4 HCAPLUS
CN Benzeneacetic acid, 3-chloro-4-(2,5-dihydro-1H-pyrrol-1-yl)-α-methyl- (9CI) (CA INDEX NAME)



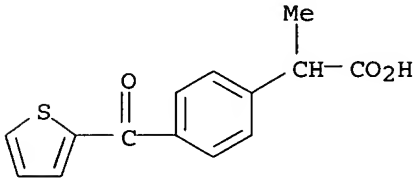
RN 31842-01-0 HCAPLUS
CN Benzeneacetic acid, 4-(1,3-dihydro-1-oxo-2H-isoindol-2-yl)-α-methyl- (9CI) (CA INDEX NAME)



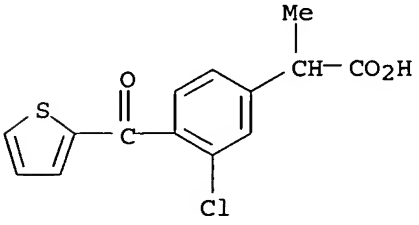
RN 34645-84-6 HCAPLUS
CN Benzeneacetic acid, 2-(2,4-dichlorophenoxy)- (9CI) (CA INDEX NAME)



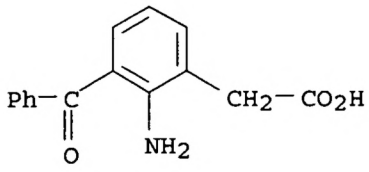
RN 40828-46-4 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



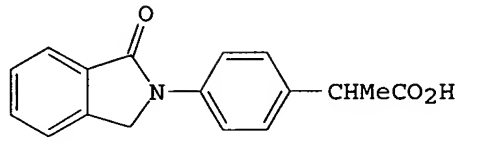
RN 51022-75-4 HCAPLUS
CN Benzeneacetic acid, 3-chloro-α-methyl-4-(2-thienylcarbonyl)- (9CI) (CA INDEX NAME)



RN 51579-82-9 HCAPLUS
CN Benzeneacetic acid, 2-amino-3-benzoyl- (9CI) (CA INDEX NAME)


Ph
C
O
NH2
CH2
CO2H

L29 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:417931 HCAPLUS
DOCUMENT NUMBER: 95:17931
TITLE: Interaction of glipizide and indoprofen
AUTHOR(S): Melander, A.; Waahlin-Boll, E.
CORPORATE SOURCE: Dep. Clin. Pharmacol., Univ. Lund, Lund, Swed.
SOURCE: European Journal of Rheumatology and Inflammation (**1981**), 4(1), 22-5
CODEN: EJRIDH; ISSN: 0140-1610
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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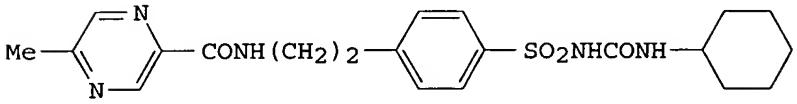


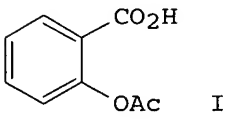
II

AB The possible kinetic and dynamic interactions of indoprofen (I) [**31842-01-0**] and glipizide (II) [29094-61-9] were investigated in healthy volunteers taking indoprofen 200 mg 3 times a day for 7 days and a single dose of glipizide 5 mg before and during indoprofen **medication.** Results suggest that indoprofen may reduce glipizide concns. in plasma, but this does not seem to influence the **blood glucose** response to glipzide.

L29 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:94 HCAPLUS
DOCUMENT NUMBER: 94:94
TITLE: The binding sites on human serum albumin for some nonsteroidal antiinflammatory drugs
AUTHOR(S): Kober, Anita; Sjoeholm, Ingvar
CORPORATE SOURCE: Biomed. Cent., Univ. Uppsala, Uppsala, S-751 23, Swed.
SOURCE: Molecular Pharmacology (**1980**), 18(3), 421-6
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 4 antiinflammatory **drugs** azapropazone [13539-59-8], flurbiprofen [**5104-49-4**], ibuprofen [**15687-27-1**], and naproxen [22204-53-1] all bind very strongly to serum albumin, with association consts., Ka, of 5.0 + 105, 5.0 + 106, 1.3 + 106, and 1.8 + 106/M, resp. The binding consts. were determined with albumin immobilized in microparticles and were in good agreement with those obtained with equilibrium dialysis. Ibuprofen, flurbiprofen, and naproxen are primarily bound to the diazepam [439-14-5] site on the albumin mol., as shown in interaction studies with albumin immobilized in microparticles. This site is shared with, e.g., some **antidiabetic** agents and benzodiazepines. Azapropazone is primarily bound to the warfarin [81-81-2] site, to which also other coumarin derivs. and, e.g., phenytoin and bilirubin are bound. The antiinflammatory **drugs** studied have small distribution vols. and low free fractions in plasma, which means that displacement from their binding sites may be of **pharmacokinetic** significance.

L29 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:115387 HCAPLUS
DOCUMENT NUMBER: 90:115387
TITLE: Aspirin stimulates insulin and glucagon secretion and increases glucose tolerance in normal and diabetic subjects
AUTHOR(S): Micossi, Piero; Pontiroli, Antonio; Baron, Steven H.; Tamayo, Raul C.; Lengel, Frieda; Bevilacqua, Maurizio; Raggi, Umberto; Norbiato, Guido; Foa, Piero P.
CORPORATE SOURCE: Dep. Res., Sinai Hosp. Detroit, Detroit, MI, USA
SOURCE: Diabetes (**1978**), 27(12), 1196-204
CODEN: DIAEAZ; ISSN: 0012-1797
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

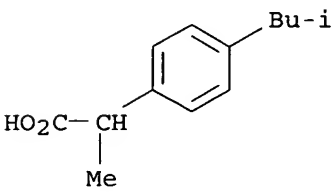


I

AB Normal subjects and patients with adult-onset **diabetes** received 10 gm of aspirin (I) [50-78-2] in 4 days. On the fourth day, the fasting serum glucose and the glucose response to oral glucose were decreased in both groups. These changes were associated with increased levels of serum insulin [9004-10-8] and pancreatic glucagon [9007-92-5], although the glucagon responses to oral glucose were unchanged. In the **diabetic** patients, I **therapy** was followed by a decreased glucose response to i.v. glucose and by the appearance of an early insulin peak, which could not be demonstrated before treatment. I did not affect the i.v. glucose tolerance in normal subjects, although it did enhance the early insulin peak. A decrease in the fasting levels of free fatty acids was noted in both groups, whereas the fasting level of triglycerides decreased only in the **diabetic** patients. Cholesterolemia did not change in either group. In normal subjects, ibuprofen [**15687-27-1**] and ketoprofen [**22071-15-4**], two other presumed prostaglandin inhibitors, did not affect fasting glycemia, glucose tolerance, or the insulin response to glucose.

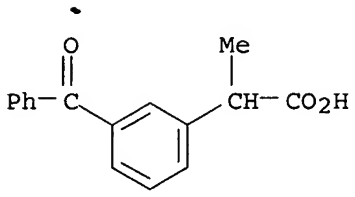
IT **15687-27-1 22071-15-4**
RL: BIOL (Biological study)
(glucagon and insulin secretion and **blood sugar** response to, in **diabetes**)

RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS

CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



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=> => d stat que l34
L1                STR
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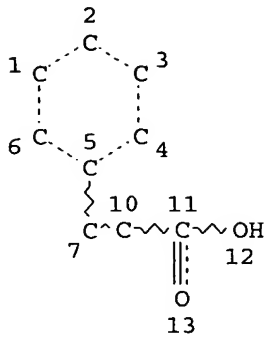


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
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L3                STR
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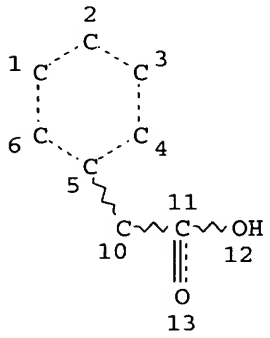


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
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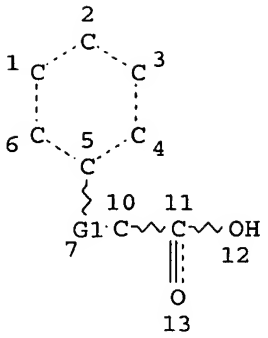

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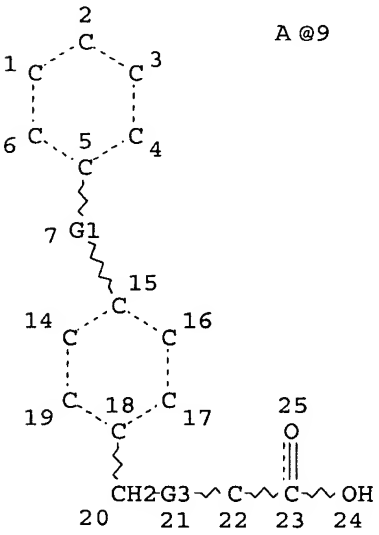
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 5
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L5 STR



REP G1=(0-1) 9
VAR G3=O/S/N
NODE ATTRIBUTES:
NSPEC IS RC AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 14 5
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
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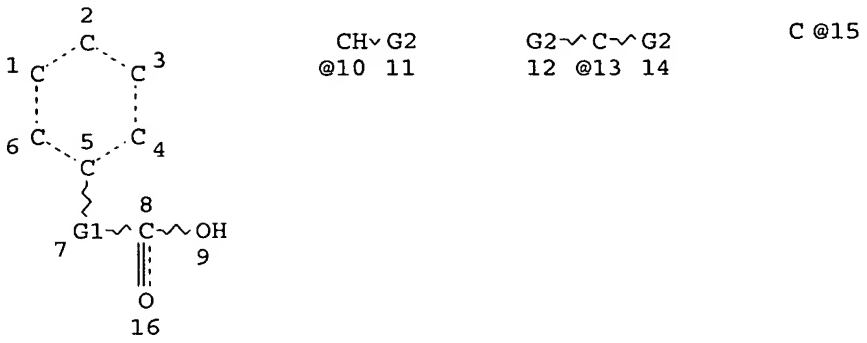
L14 204237 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DIABETES MELLITUS"/CV OR DIABETES/CV) OR "ANTIDIABETIC AGENTS"/CV OR HYPERGLYCEMIA/CV OR ?DIABET? OR ?HYPERGLYCEM? OR (BLD OR BLOOD)(2A)(SUGAR OR GLUCOSE) OR MUSCULAR DYSTROPHY/CV OR DYSTROPHY/CV OR MYODYSTROPHY/CV OR ?DYSTROPHY? OR ?SCLEROS?(2A)SYSTEM?

L19 STR



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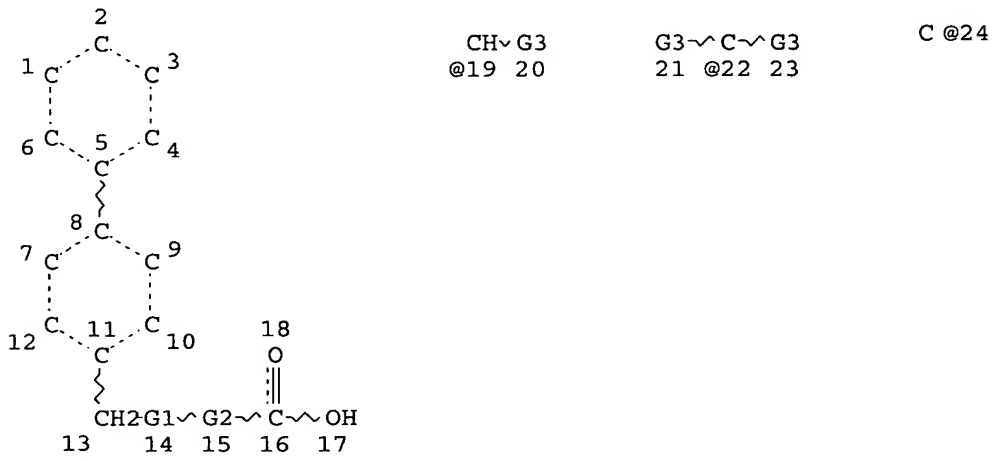
VAR G2=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L20 STR



VAR G1=O/S/NH/SO2
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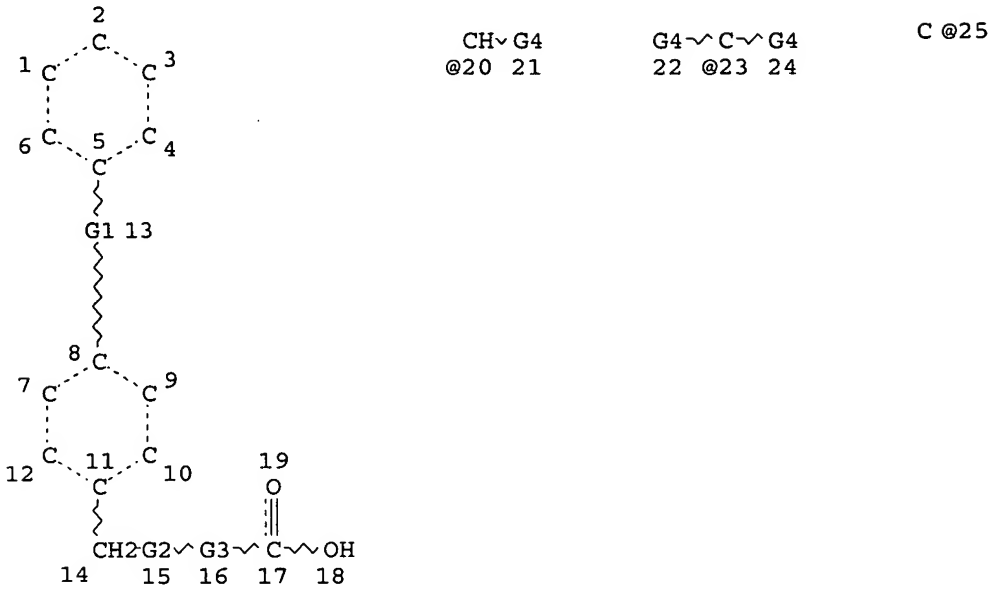
VAR G3=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L21 STR



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VAR G2=O/S/NH/SO2
VAR G3=CH2/20/23/25
VAR G4=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
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L24 27972 SEA FILE=REGISTRY SUB=L22 SSS FUL L19 OR L20 OR L21
L25 58477 SEA FILE=HCAPLUS ABB=ON PLU=ON L24
L26 283 SEA FILE=HCAPLUS ABB=ON PLU=ON L14(L)L25
L27 114 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND PD=<MAY 28, 1999
L28 7507 SEA FILE=HCAPLUS ABB=ON PLU=ON L25(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR ?PHARMA?)
L29 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L28
L30 1470 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L25
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L32 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND L31
L33 48 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 NOT L29
L34 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L33 AND PATENT/DT

=>
=>

=> d ibib abs hitstr l34 1-37

L34 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:462814 HCAPLUS
DOCUMENT NUMBER: 141:17635
TITLE: Method of treating neurological diseases and etiologically related symptomology using carbonyl trapping agents in combination with medicaments
INVENTOR(S): Shapiro, Howard K.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 883,290, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

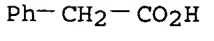
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6746678	B1	20040608	US 2000-545870	20000406
US 5668117	A	19970916	US 1993-62201	19930629 <--

PRIORITY APPLN. INFO.:
US 1991-660561 B1 19910222
US 1993-26617 B2 19930223
US 1993-62201 A2 19930629
US 1997-883290 B2 19970626

OTHER SOURCE(S): MARPAT 141:17635

AB The invention discloses a method for treatment of several neurol. diseases and pathophysiol. related symptomol., the diseases including peripheral neuropathies, secondary symptomol. of **diabetes**, Alzheimer's disease, Parkinson's disease, alc. polyneuropathy and age-onset symptomol., as well as analogous veterinary disease states. An opportunity exists for pharmacol. intervention in some neurol. diseases by use of water-soluble, small-mol.-weight primary amine agents and chemical derivs.
thereof. Examples of such primary pharmacol. agents include 4-aminobenzoic acid and derivs. thereof. The invention also includes: (1) oral use of optional nonabsorbable polyamine polymeric co-agents, e.g. chitosan, (2) oral use of optional known antioxidant co-agents and related nutritional factors, and (3) use of the primary agents and above co-agents in optional combination with medicaments recognized as effective for treatment of the diseases addressed herein or symptoms thereof.

IT **103-82-2D**, Phenylacetic acid, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbonyl trapping agents in combination with **medicaments** for treatment of neurol. diseases and etiol. related symptomol.)
RN 103-82-2 HCAPLUS
CN Benzeneacetic acid (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:392219 HCAPLUS
DOCUMENT NUMBER: 136:406945
TITLE: Methods for in vivo drug delivery based on monitoring blood flow parameters
INVENTOR(S): Kensey, Kenneth R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 727,950.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061835	A1	20020523	US 2001-828761	20010409
US 6019735	A	20000201	US 1997-919906	19970828
CA 2301161	AA	19990304	CA 1998-2301161	19980826 <--
NZ 502905	A	20010831	NZ 1998-502905	19980826
JP 2001514384	T2	20010911	JP 2000-507994	19980826
US 6322524	B1	20011127	US 1999-439795	19991112
US 6322525	B1	20011127	US 2000-501856	20000210
NO 2000000944	A	20000225	NO 2000-944	20000225
US 6428488	B1	20020806	US 2000-615340	20000712
WO 2002043806	A2	20020606	WO 2001-US44352	20011127
WO 2002043806	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002026986	A5	20020611	AU 2002-26986	20011127
US 2002088953	A1	20020711	US 2001-33841	20011227
US 6624435	B2	20030923		
WO 2002079778	A2	20021010	WO 2002-US3984	20020207
WO 2002079778	A3	20030710		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002184941	A1	20021212	US 2002-156165	20020528
US 6571608	B2	20030603		

PRIORITY APPLN. INFO.:

US 1997-919906	A2 19970828
US 1999-439795	A2 19991112
US 2000-501856	A2 20000210
US 2000-628401	A2 20000801
US 2000-727950	A2 20001201

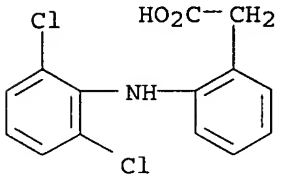
US 1997-966076	A	19971107
WO 1998-US17657	W	19980826
US 2000-615340	A3	20000712
US 2000-228612P	P	20000828
US 2001-789350	B2	20010221
US 2001-819924	A	20010328
US 2001-828761	A	20010409
US 2001-839785	A	20010420
US 2001-841389	A	20010424
US 2001-897164	A3	20010702
WO 2001-US44352	W	20011127

AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being over a range of shear rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream.

IT **15307-86-5**, Diclofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for in vivo **drug** delivery based on monitoring blood flow parameters)

RN 15307-86-5 HCAPLUS

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

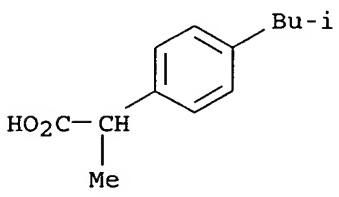


L34 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:213707 HCAPLUS
DOCUMENT NUMBER: 136:252489
TITLE: Sustained-release polymer blend for pharmaceutical applications
INVENTOR(S): Guo, Jian Hwa; Skinner, George William
PATENT ASSIGNEE(S): Hercules Incorporated, USA
SOURCE: U.S., 9 pp., Cont.-in-part of U.S. 6,210,710.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6358525	B1	20020319	US 1999-343425	19990630
US 6210710	B1	20010403	US 1997-847842	19970428
NO 9801893	A	19981029	NO 1998-1893	19980427 <--
PRIORITY APPLN. INFO.:			US 1997-847842 A2	19970428

AB A pharmaceutical composition has a blend of at least first and second components and a medicament in a sufficient amount to be therapeutic where the first component is hydroxypropylcellulose and the second component is at least one other polymer selected from the group consisting of methylcellulose, ethylhydroxyethylcellulose, hydroxyethylmethylcellulose, hydrophobically modified hydroxyethylcellulose, hydrophobically modified ethylhydroxyethylcellulose, carboxymethylhydroxyethylcellulose, carboxymethyl hydrophobically modified hydroxyethylcellulose, guar, pectin, carrageenan, agar, algin, gellan gum, acacia, starch and modified starches, co-polymers of carboxyvinyl monomers, co-polymers of acrylate or methacrylate monomers, mono- and co-polymers of oxyethylene and oxypropylene and mixts. thereof and a medicament in a sufficient amount to be therapeutic, with the proviso that low-substituted hydroxypropylcellulose is excluded from said first and second components. The medicament can be a variety of drugs or nutritional supplements. The pharmaceutical composition releases the medicament for a prolonged or sustained period of time and can be formulated into many dosage forms. A tablet contained Klucel HXF 37.5, Aqualon CMC 7L2P 112.5, phenylpropanolamine hydrochloride 75, avicel PH-101 162, povidone 12, reduced granulation 299, Avicel PH-102 96, magnesium starate 5%.

IT **15687-27-1**, Ibuprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained-release polymer blend for **pharmaceutical** applications)
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:185688 HCAPLUS
DOCUMENT NUMBER: 136:252567
TITLE: Methods for drug administration and distribution based on monitoring blood viscosity and other parameters for diagnostics and treatment
INVENTOR(S): Kensey, Kenneth
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 819,924.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002032149	A1	20020314	US 2001-841389	20010424
US 6019735	A	20000201	US 1997-919906	19970828
CA 2301161	AA	19990304	CA 1998-2301161	19980826 <--
NZ 502905	A	20010831	NZ 1998-502905	19980826
JP 2001514384	T2	20010911	JP 2000-507994	19980826
US 6322524	B1	20011127	US 1999-439795	19991112
US 6322525	B1	20011127	US 2000-501856	20000210
NO 2000000944	A	20000225	NO 2000-944	20000225
US 6428488	B1	20020806	US 2000-615340	20000712
US 2002088953	A1	20020711	US 2001-33841	20011227
US 6624435	B2	20030923		
WO 2002079778	A2	20021010	WO 2002-US3984	20020207
WO 2002079778	A3	20030710		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002184941	A1	20021212	US 2002-156165	20020528
US 6571608	B2	20030603		

PRIORITY APPLN. INFO.:

US 1997-919906	A2	19970828
US 1999-439795	A2	19991112
US 2000-501856	A2	20000210
US 2000-628401	A2	20000801
US 2000-727950	A2	20001201
US 2001-819924	A2	20010328
US 1997-966076	A	19971107
WO 1998-US17657	W	19980826
US 2000-615340	A3	20000712
US 2000-228612P	P	20000828
US 2001-789350	B2	20010221
US 2001-828761	A	20010409
US 2001-839785	A	20010420
US 2001-841389	A	20010424
US 2001-897164	A3	20010702

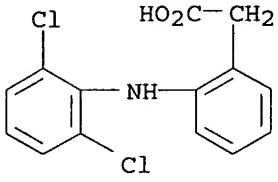
AB Various methods are provided for determining and utilizing the viscosity of the circulating blood of a living being, i.e., a human, over a range of shear

rates for diagnostics and treatment, such as detecting/reducing blood viscosity, work of the heart, contractility of the heart, for detecting/reducing the surface tension of the blood, for detecting plasma viscosity, for explaining/countering endothelial cell dysfunction, for providing high and low blood vessel wall shear stress data, red blood cell deformability data, lubricity of blood, and for treating different ailments such as peripheral arterial disease in combination with administering to a living being at least one pharmaceutically acceptable agent. Agents pharmaceutically effective to regulate at least one of the aforementioned blood parameters are used to adjust distribution of a substance through the bloodstream. For example, when blood viscosity is a blood flow parameter monitored, an agent is selected from i.v. diluents, red blood cell deformability agents, antiurea agents, oral contraceptives, **antidiabetic** agents, antiarrhythmics, antihypertensives, antihyperlipidemics, antiplatelet agents, appetite suppressants, antiobesity agents, blood modifiers, smoking deterrent agents, and nutritional supplements.

IT **15307-86-5**, Diclofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apparatus and methods for monitoring blood viscosity and other parameters in **drug** delivery for diagnostics and treatment)

RN 15307-86-5 HCAPLUS

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



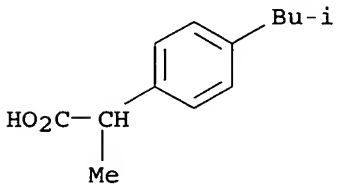
L34 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:489846 HCAPLUS
DOCUMENT NUMBER: 135:82020
TITLE: Formulations for therapeutic agents absorbed through mucous membranes
INVENTOR(S): Liversidge, Gary G.; Eickhoff, W. Mark; Illig, Kathleen J.; Sarpotdar, Pramod; Ruddy, Stephen B.
PATENT ASSIGNEE(S): Elan Pharma International Limited, USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. 5,628,981.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001006617	A1	20010705	US 1997-815346	19970311
US 6432381	B2	20020813		
US 5628981	A	19970513	US 1994-366841	19941230 <--
US 2003054045	A1	20030320	US 2002-175851	20020621
US 2005004049	A1	20050106	US 2003-683154	20031014
PRIORITY APPLN. INFO.:			US 1994-366841	A2 19941230
			US 1997-815346	A1 19970311
			US 2002-175851	B2 20020621

AB Particulate crystalline therapeutic substances are formulated with stabilizers to enhance contact between the crystalline therapeutic substances and the mucosal membranes to provide extended therapeutic effect. A composition containing paclitaxol having specified particle size 10, Pluronic F108 5, sodium benzoate 0.2, sodium saccharin 0.1, FD & C Red Nol. 40 0.03 g and water q.s. to 100 mL was formulated.

IT **15687-27-1**, Ibuprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations for **therapeutic** agents absorbed through mucous membranes containing poloxamers)

RN 15687-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



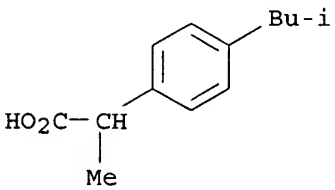
L34 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:279528 HCAPLUS
DOCUMENT NUMBER: 134:300794
TITLE: Sustained release polymer blend for pharmaceutical applications
INVENTOR(S): Skinner, George William
PATENT ASSIGNEE(S): Hercules Inc., USA
SOURCE: U.S., 9 pp., Cont.-in-part of U.S. Ser. No. 847,842.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6217903	B1	20010417	US 1999-343860	19990630
US 6210710	B1	20010403	US 1997-847842	19970428
NO 9801893	A	19981029	NO 1998-1893	19980427 <--

PRIORITY APPLN. INFO.: US 1997-847842 A2 19970428

AB A pharmaceutical composition has a blend of at least first and second components and a medicament in a sufficient amount to be therapeutic where the first component is Et cellulose (EC) and the second component is at least one other polymer selected from the group consisting of Me cellulose (MC), Et hydroxyethyl cellulose (EHEC), hydroxyethyl Me cellulose (HEMC), hydrophobically modified hydroxyethyl cellulose (HMHEC), hydrophobically modified Et hydroxyethyl cellulose (HMEHEC), carboxymethyl hydroxyethyl cellulose (CMHEC), carboxymethyl hydrophobically modified hydroxyethyl cellulose (CMHMHEC), guar, pectin, carrageenan, agar, algin, gellan gum, acacia, starch and modified starches, mono- and co-polymers of carboxyvinyl monomers, mono- and co-polymers of acrylate or methacrylate monomers, mono- and co-polymers of oxyethylene and oxypropylene and mixts. thereof. The medicament can be a variety of drugs or nutritional supplements. The pharmaceutical composition releases the medicament for a prolonged or sustained period of time. For example, tablets of a model drug phenylpropanolamine monohydrochloride (PPA) were prepared by blending (a) a wet granulation containing Klucel HXF 37.57 mg, Aqualon CMC 7L2P 112.5 mg, PPA 75 mg, Avicel PH-101 162 mg, and Povidone 12 mg, and (b) a dried/reduced granulation 399 mg, Avicel PH-102 96 mg, and Mg stearate 5 mg.

IT **15687-27-1**, Ibuprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymer blends for sustained release of **drugs** and nutritional supplements)
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:420917 HCAPLUS
DOCUMENT NUMBER: 133:48889
TITLE: Chewing gum containing medicament active agents
INVENTOR(S): McGrew, Gordon N.; Barkalow, David G.; Johnson, Sonya S.; Record, David W.; Patel, Mansukh M.; Nimz, Jack D.; Zibell, Steven E.; Yatka, Robert J.; Greenberg, Michael J.; Aumann, Rebecca A.; Zyck, Daniel J.; Sitler, Daniel J.; Hook, Jeffrey S.; Maxwell, James R.; Reed, Michael A.; Gudas, Victor V.; Schnell, Philip G.; Tyrpin, Henry T.; Russell, Michael P.; Witkewitz, David L.; Song, Joo H.; Townsend, Donald J.; Seielstad, Donald A.
PATENT ASSIGNEE(S): Wm. Wrigley Jr. Company, USA; et al.
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035298	A1	20000622	WO 1999-US29792	19991214
W: US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2271889	AA	19980604	CA 1996-2271889	19961127 <--
CA 2271889	C	20040127		
CA 2431848	AA	19980604	CA 1996-2431848	19961127 <--
CA 2431856	AA	19980604	CA 1996-2431856	19961127 <--
WO 9823165	A1	19980604	WO 1996-US18977	19961127 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
AU 9712745	A1	19980622	AU 1997-12745	19961127 <--
CA 2272703	AA	19980604	CA 1996-2272703	19961223 <--
CA 2272703	C	20020924		
AU 9717432	A1	19980622	AU 1997-17432	19961223 <--
AU 719781	B2	20000518		
EP 967883	A1	20000105	EP 1996-945948	19961223
EP 967883	B1	20030924		
R: DE, DK, FR, GB				
US 6165516	A	20001226	US 1999-308972	19990527
BR 9916304	A	20011113	BR 1999-16304	19991214
EP 1221863	A1	20020717	EP 1999-966283	19991214
R: DE, DK, FR, GB, IT, NL				
US 6949264	B1	20050927	US 2000-621780	20000721
US 6444241	B1	20020903	US 2000-651514	20000830
US 6531114	B1	20030311	US 2000-714571	20001116
EP 1347746	A1	20031001	EP 2001-953503	20010717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002164398	A1	20021107	US 2001-24631	20011217
AU 773949	B2	20040610	AU 2002-23197	20020308
US 2003180414	A1	20030925	US 2002-280688	20021025
AU 2004233478	A1	20041223	AU 2004-233478	20041125

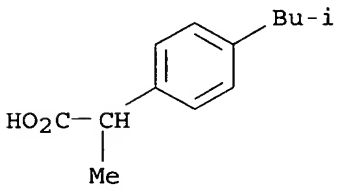
PRIORITY APPLN. INFO.:

WO 1996-US18977	A2	19961127
US 1998-112389P	P	19981215
US 1999-308972	A2	19990527
US 1999-389211	A2	19990902
CA 1996-2271889	A3	19961127
AU 1997-13382	A3	19961223
WO 1996-US20252	W	19961223
WO 1996-US20329	W	19961223
US 1999-286618	A2	19990406
US 1999-286818	A	19990406
US 1999-319054	A2	19990526
WO 1999-US29742	A1	19991214
WO 1999-US29792	W	19991214
US 2000-621780	A2	20000721
US 2001-888057	A2	20010622
WO 2001-US22360	W	20010717
AU 2002-21302	A3	20020306

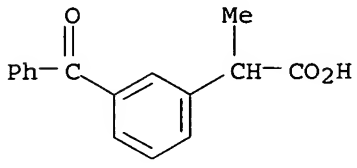
AB A method for producing a chewing gum with a controlled release active agent, as well as the chewing gum so produced, is obtained by phys. modifying the release properties of the active agent by coating and drying. The active agent is coated by encapsulation, partially coated by agglomeration, entrapped by absorption, or treated by multiple steps of encapsulation, agglomeration, and absorption. The coated active agent is preferably then co-dried and particle sized to produce a release-modified active agent for use in chewing gum. The active agent may also be used in a coating on a chewing gum product, as part of a rolling compound applied to the chewing gum product, or as a part of the liquid in a liquid-center chewing gum product. A composition contained sugar 62.5, base 19.2, corn syrup 15.9, peppermint flavor 0.9, glycerin 1.4, and liquid/drug (e.g., dyclonine-HCl) blend 0.1 weight%.

IT **15687-27-1**, Ibuprofen **22071-15-4**, Ketoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chewing gum for controlled **drug** release)

RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:420916 HCAPLUS
DOCUMENT NUMBER: 133:48888
TITLE: Improved release of medicament active agents from a chewing gum coating
INVENTOR(S): Johnson, Sonya S.; Record, David W.; Greenberg, Michael J.; Reed, Michael A.; Gudas, Victor V.; Schnell, Philip G.; Seielstad, Donald A.; Typrin, Henry T.; Russell, Michael P.; Witkewitz, David L.; Song, Joo H.; Townsend, Donald J.; Yatka, Robert J.; Ream, Ronald L.; Corriveau, Christine L.; Wokas, William J.
PATENT ASSIGNEE(S): Wm. Wrigley Jr. Co., USA; et al.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035296	A1	20000622	WO 1999-US29742	19991214
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2271889	AA	19980604	CA 1996-2271889	19961127 <--
CA 2271889	C	20040127		
CA 2431848	AA	19980604	CA 1996-2431848	19961127 <--
CA 2431856	AA	19980604	CA 1996-2431856	19961127 <--
WO 9823165	A1	19980604	WO 1996-US18977	19961127 <--
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AU 9712745	A1	19980622	AU 1997-12745	19961127 <--
CA 2272703	AA	19980604	CA 1996-2272703	19961223 <--
CA 2272703	C	20020924		
AU 9717432	A1	19980622	AU 1997-17432	19961223 <--
AU 719781	B2	20000518		
EP 967883	A1	20000105	EP 1996-945948	19961223
EP 967883	B1	20030924		
R: DE, DK, FR, GB				
US 6165516	A	20001226	US 1999-308972	19990527
CA 2355779	AA	20000622	CA 1999-2355779	19991214
CA 2355779	C	20060207		
AU 2000021843	A5	20000703	AU 2000-21843	19991214
AU 765999	B2	20031009		
BR 9916303	A	20011002	BR 1999-16303	19991214
EP 1139774	A1	20011010	EP 1999-966257	19991214
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US 6355265	B1	20020312	US 2000-510878	20000223

US 6322806	B1	20011127	US 2000-618808	20000718
US 6627234	B1	20030930	US 2000-621643	20000721
US 6444241	B1	20020903	US 2000-651514	20000830
US 2001024642	A1	20010927	US 2001-759561	20010111
US 6558692	B2	20030506		
EP 1347746	A1	20031001	EP 2001-953503	20010717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002012633	A1	20020131	US 2001-956445	20010919
US 6592850	B2	20030715		
US 6426090	B1	20020730	US 2001-955870	20010919
US 2002159956	A1	20021031	US 2001-990628	20011113
US 2003049208	A1	20030313	US 2001-992122	20011113
US 6773716	B2	20040810		
US 2002164398	A1	20021107	US 2001-24631	20011217
AU 773949	B2	20040610	AU 2002-23197	20020308
US 2004180007	A1	20040916	US 2003-743609	20031222
AU 2004233478	A1	20041223	AU 2004-233478	20041125

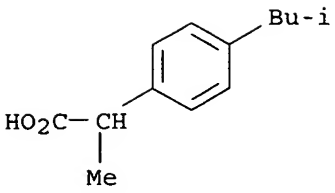
PRIORITY APPLN. INFO.:	WO 1996-US18977	A2 19961127
	US 1998-112389P	P 19981215
	US 1999-286818	A 19990406
	US 1999-308972	A2 19990527
	US 1999-389211	A2 19990902
	CA 1996-2271889	A3 19961127
	AU 1997-13382	A3 19961223
	WO 1996-US20329	W 19961223
	WO 1999-US29742	W 19991214
	WO 1999-US29792	A1 19991214
	US 2000-510878	A2 20000223
	US 2000-618808	A2 20000718
	US 2000-621780	A2 20000721
	US 2000-631326	A3 20000803
	US 2000-671552	B1 20000927
	US 2000-714571	A3 20001116
	US 2001-888057	A2 20010622
	WO 2001-US22360	W 20010717
	AU 2002-21302	A3 20020306

AB A method for producing a chewing gum with an improved release of active agent, as well as the chewing gum so produced, is obtained by adding an active agent to a chewing gum coating. The active agent is added to the coating in a coating solution or premixed with a flavor or solvent. The coating solution may contain sweetener or other transdermal enhancing agents to obtain increased transmucosal absorption. An active agent may also be used in the gum core. Formulations, e.g., sugar 48.7, gum base 30.0, corn syrup 19.0, glycerin 1.0, peppermint flavor 1.0 and dyclonin-HCl 0.3 weight % were given.

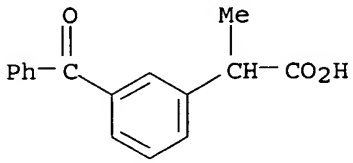
IT **15687-27-1**, Ibuprofen **22071-15-4**, Ketoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved **drug** release from a chewing gum coating)

RN 15687-27-1 HCAPLUS

CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



L34 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:412670 HCAPLUS
DOCUMENT NUMBER: 131:54044
TITLE: Compositions comprising nicotinylalanine and an inhibitor of glycine conjugation or vitamin B6, and therapeutic use
INVENTOR(S): Shaskan, Edward G.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 581,394, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

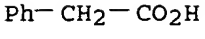
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5916906	A	19990629	US 1997-930234	19970912
WO 9628167	A1	19960919	WO 1996-US3435	19960313 <--

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

PRIORITY APPLN. INFO.: US 1995-403676 B2 19950314
US 1995-581394 B2 19951229
WO 1996-US3435 W 19960313
OTHER SOURCE(S): MARPAT 131:54044

AB Compns. are provided which comprise nicotinylalanine (NAL) and/or related analogs, and an inhibitor of glycine conjugation, either synthetic or naturally occurring. Vitamin B6 may also be present in the compns.in place of, or in addition to, the inhibitor of glycine conjugation. The compns. may be pharmaceutical in nature. The compns. are useful for inhibiting cellular poly(ADP-ribose) polymerase (PARP, PARS, poly(ADP-ribose) synthetase), an enzyme which causes cellular toxicity and which is activated in a variety of toxic and pathol. conditions. PARP is inhibited by some metabolites of the tryptophan oxidative pathway, including nicotinamide, kynurenic acid and xanthurenic acid, which are induced by interferon-gamma. The NAL-containing compns. of the invention enhance the intracellular levels of these metabolites, and thereby augment the natural defense of interferon-induced inhibition of PARP. PARP is implicated in various pathol. conditions, including neurodegenerative disorders, viral infections such as AIDS, autoimmune diseases and cancer. Accordingly, the invention also relates to methods of reducing cellular toxicity, and treating or preventing such diseases, by increasing cellular concns. of nicotinamide, kynurenic acid and xanthurenic acid using the compns. of this invention.

IT **114-70-5**, Sodium phenylacetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising nicotinylalanine and an inhibitor of glycine conjugation or vitamin B6, and **therapeutic** use)
RN 114-70-5 HCAPLUS
CN Benzeneacetic acid, sodium salt (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:292567 HCAPLUS
DOCUMENT NUMBER: 130:329203
TITLE: Drug composition with controlled drug release rate comprising hyaluronate and biodegradable polymers
INVENTOR(S): Suzuki, Makoto; Ishigaki, Kenji; Okada, Minoru; Ono, Kenji; Kasai, Shuichi; Imamori, Katsumi
PATENT ASSIGNEE(S): SSP Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

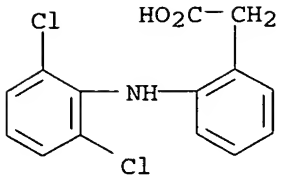
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 913149	A1	19990506	EP 1998-119415	19981014 <--
EP 913149	B1	20050309		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11130697	A2	19990518	JP 1997-294008	19971027 <--
TW 520292	B	20030211	TW 1998-87116892	19981012
US 6375988	B1	20020423	US 1998-172270	19981014
ES 2239376	T3	20050916	ES 1998-119415	19981014
CA 2251281	AA	19990427	CA 1998-2251281	19981020 <--
CN 1220874	A	19990630	CN 1998-122614	19981027
HK 1019142	A1	20040716	HK 1999-104382	19991007

PRIORITY APPLN. INFO.: JP 1997-294008 A 19971027

AB A drug composition with a controlled drug release rate is disclosed. The drug composition comprises (a) a biodegradable, biocompatible high-mol. substance and/or polyvalent metal ions or polyvalent metal ion source, and (b) hyaluronic acid or a salt thereof; and a drug incorporated as an ingredient (c) in said matrix. The drug composition has biodegradability and biocompatibility, permits easy control of a release rate of the drug, and can persistently exhibit its pharmacol. effect over a long time. A solution of 1% sodium hyaluronate (I)was added to 200 mg medium-chain fatty acid triglyceride and the mixture was stirred followed by addition of 50% aqueous calcium chloride solution The microspheres thus obtained were separated, washed, and dried. The microspheres had an average particle size of 78.4 μm and I content of 78.1%.

IT **15307-79-6**, Sodium diclofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**drug** composition with controlled **drug** release rate comprising hyaluronate and biodegradable polymers)

RN 15307-79-6 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)



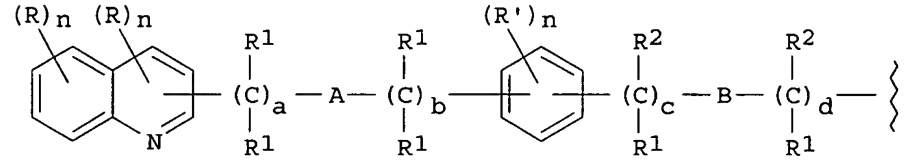
● Na

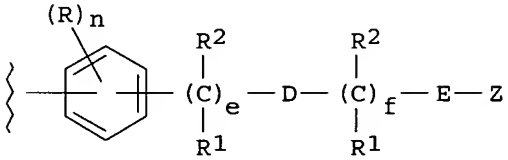
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:282096 HCAPLUS
DOCUMENT NUMBER: 130:320864
TITLE: PPAR-γ-binding quinoline derivatives, their preparation, and their therapeutic use
INVENTOR(S): Jayyosi, Zaid; McGeehan, Gerard M.; Kelley, Michael F.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9920275	A1	19990429	WO 1998-US21947		19981016 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2306825	AA	19990429	CA 1998-2306825		19981016 <--
AU 9896961	A1	19990510	AU 1998-96961		19981016 <--
ZA 9809465	A	20000417	ZA 1998-9465		19981016
EP 1030665	A1	20000830	EP 1998-951075		19981016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO					
BR 9814087	A	20001003	BR 1998-14087		19981016
JP 2001520193	T2	20011030	JP 2000-516672		19981016
US 6376512	B1	20020423	US 2000-490897		20000127
NO 2000001962	A	20000616	NO 2000-1962		20000414
BG 104432	A	20001229	BG 2000-104432		20000515
PRIORITY APPLN. INFO.:			US 1997-62318P	P	19971017
			US 1997-65902P	P	19971117
			WO 1998-US21947	W	19981016

OTHER SOURCE(S): MARPAT 130:320864
GI



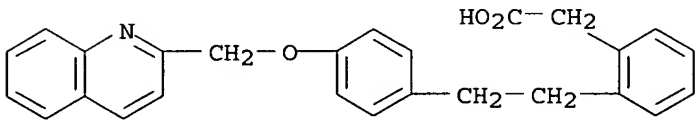


I

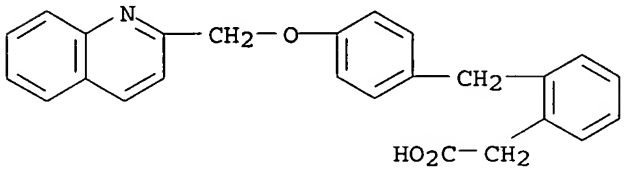
AB A method for mediating the activity of PPAR-γ receptor comprises contacting the PPAR-γ receptor with I [A = O, S, (R1)C=C(R1), bond; B = O, S, SO, SO2, NR1, bond; D = O, S, NR1, (R1)C=C(R1), bond; E = bond; a = 0-2; b = 0, 1; c = 0-4; d = 0-5; e = 0-4; f = 0-5; n = 0-2; R = H; R' = H; R1 = H; R2 = (CH2)qX, or two vicinal R2 taken together with the carbon atoms through which the two vicinal R2 are linked form cycloalkylene, etc.; q = 0-3; X = H]. Preparation of I is described. The compds. may be used to treat cardiovascular conditions, **diabetes**, hyperlipidemia, hypertension, eating disorders, etc.

IT **123692-37-5P 123692-38-6P 223772-12-1P 223772-18-7P 223772-43-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PPAR-γ-binding quinoline derivative preparation and **therapeutic** use)

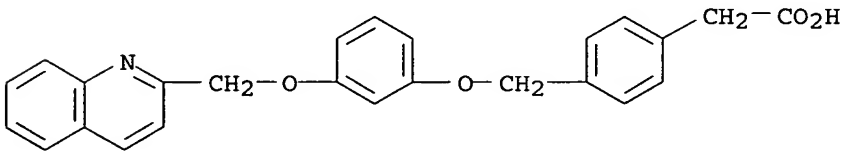
RN 123692-37-5 HCAPLUS
CN Benzeneacetic acid, 2-[2-[4-(2-quinolinylmethoxy)phenyl]ethyl]- (9CI) (CA INDEX NAME)



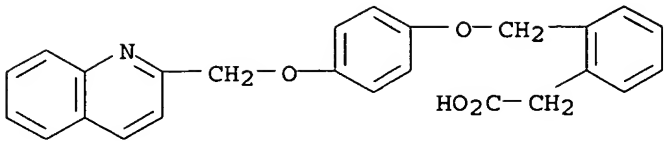
RN 123692-38-6 HCAPLUS
CN Benzeneacetic acid, 2-[[4-(2-quinolinylmethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



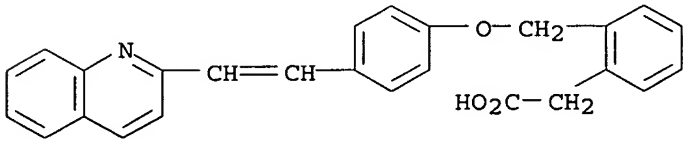
RN 223772-12-1 HCAPLUS
CN Benzeneacetic acid, 4-[[3-(2-quinolinylmethoxy)phenoxy]methyl]- (9CI) (CA INDEX NAME)



RN 223772-18-7 HCAPLUS
CN Benzeneacetic acid, 2-[[4-(2-quinolinylmethoxy)phenoxy]methyl]- (9CI) (CA INDEX NAME)



RN 223772-43-8 HCAPLUS
CN Benzeneacetic acid, 2-[[4-[2-(2-quinolinyl)ethenyl]phenoxy]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:806633 HCAPLUS
DOCUMENT NUMBER: 130:57211
TITLE: Preparation of conjugates of dithiocarbamates with drugs
INVENTOR(S): Lai, Ching-san
PATENT ASSIGNEE(S): Medinox, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9855453	A1	19981210	WO 1998-US10295	19980519 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5916910	A	19990629	US 1997-869158	19970604
CA 2292478	AA	19981210	CA 1998-2292478	19980519 <--
AU 9875828	A1	19981221	AU 1998-75828	19980519 <--
AU 743205	B2	20020124		
EP 1001932	A1	20000524	EP 1998-923563	19980519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511858	T2	20020416	JP 1999-502493	19980519
US 6407135	B1	20020618	US 1999-453608	19991203
US 2003087840	A1	20030508	US 2002-176396	20020618

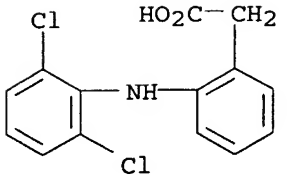
PRIORITY APPLN. INFO.:

US 1997-869158	A1	19970604
WO 1998-US10295	W	19980519
US 1999-453608	A3	19991203

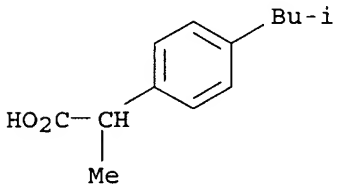
AB In accordance with the present invention, there are provided conjugates of nitric oxide scavengers (e.g., dithiocarbamates, or "DC") and drugs (e.g., NSAIDs). These conjugates provide a new class of drugs (e.g., anti-inflammatory agents) which cause a much lower incidence of side-effects due to the protective effects imparted by modifying them. The conjugates are more effective than unmodified drugs because cells and tissues contacted by them are protected from the potentially damaging effects of nitric oxide overprodn. induced as a result of the co-production of nitric oxide scavenger (e.g., dithiocarbamate), in addition to free drugs, when the conjugate is cleaved. Thus, ibuprofen was esterified with 2-pyrrolidinol in the presence of DCC, and the resulting ester was treated with aqueous NaOH solution and CS2 in EtOH solution The final product, a dithiocarbamate of pyrrolidinol-ibuprofen, was obtained in 70% yield.

IT **15307-86-5D**, dithiocarbamate conjugates **15687-27-1D**, dithiocarbamate conjugates **22071-15-4D**, dithiocarbamate conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of conjugates of dithiocarbamates with **drugs**)

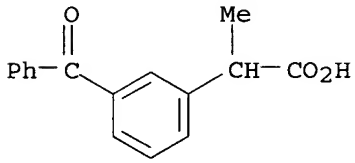
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



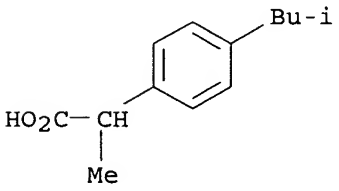
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



IT **15687-27-1**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of conjugates of dithiocarbamates with **drugs**)
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



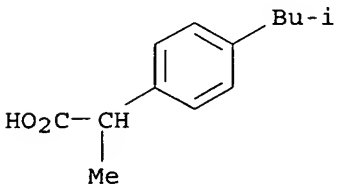
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:766507 HCAPLUS
DOCUMENT NUMBER: 130:29221
TITLE: Preparation of solid porous matrixes for pharmaceutical uses
INVENTOR(S): Unger, Evan C.
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851282	A1	19981119	WO 1998-US9570	19980512 <--
W: AU, BR, CA, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2002039594	A1	20020404	US 1998-75477	19980511
AU 9873787	A1	19981208	AU 1998-73787	19980512 <--
EP 983060	A1	20000308	EP 1998-921109	19980512
R: DE, FR, GB, IT, NL				
US 2001018072	A1	20010830	US 2001-828762	20010409
US 2004091541	A1	20040513	US 2003-622027	20030716

PRIORITY APPLN. INFO.:		
US 1997-46379P	P	19970513
US 1998-75477	A	19980511
WO 1998-US9570	W	19980512
US 2001-828762	B1	20010409

AB A solid porous matrix formed from a surfactant, a solvent, and a bioactive agent is described. Thus, amphotericin nanoparticles were prepared by using ZrO2 beads and a surfactant. The mixture was milled for 24 h.
IT **15687-27-1**, Ibuprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of solid porous matrixes for **pharmaceutical** uses)
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

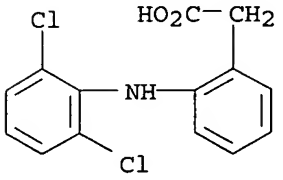
L34 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:724148 HCAPLUS
DOCUMENT NUMBER: 129:335800
TITLE: Sustained-release pharmaceutical microcapsules and their manufacture
INVENTOR(S): Fujita, Shigeki; Azumaya, Toshio; Takiyama, Mitsumasa
PATENT ASSIGNEE(S): Towa Yakuhin K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10298064	A2	19981110	JP 1997-123121	19970425 <--
PRIORITY APPLN. INFO.:			JP 1997-123121	19970425

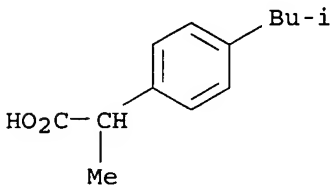
AB The title microcapsules are manufactured by emulsifying molten waxes containing higher fatty acid esters and dispersed pharmacol. active substances in H2O heated to temps. higher than the m.ps. of the waxes and then cooling the emulsions to solidify the waxes. The microcapsules are manufactured in the simple process without using organic solvents. Theophylline (I) was blended with a molten mixture of cetostearyl alc. and sucrose stearate (Ryoto Sugar Ester S 370), the mixture was emulsified in an aqueous solution (at 70-75°) containing sucrose, and cooled to give spherical microcapsules, which showed sustained-release of I for >12 h in H2O and buffers (pH 1.2, 4.0, and 6.8).

IT **15307-86-5**, Diclofenac **15687-27-1**, Ibuprofen
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(manufacture of sustained-release **pharmaceutical** microcapsules with waxes containing higher fatty acid esters)

RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



L34 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:653540 HCAPLUS
DOCUMENT NUMBER: 129:255000
TITLE: Clearing of atherosclerosis with pharmaceutical composition containing a chelating agent, a nonsteroidal antiinflammatory drug, an antioxidant, and hyaluronic acid or a hyaluronic acid salt or derivative
INVENTOR(S): Falk, Rudolf Edgar; Asculai, Samuel Simon
PATENT ASSIGNEE(S): Hyal Pharmaceutical Corporation, Can.
SOURCE: U.S., 5 pp., Cont.-in-part of U.S. Ser. No. 675,908.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817642	A	19981006	US 1995-464769	19950815 <--
CZ 288292	B6	20010516	CZ 1990-4598	19900921
US 6069135	A	20000530	US 1991-675908	19910703
CA 2122551	AA	19951030	CA 1994-2122551	19940429 <--
US 5827834	A	19981027	US 1994-286263	19940805 <--
WO 9529683	A1	19951109	WO 1995-CA243	19950427 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5811410	A	19980922	US 1995-465335	19950605 <--
US 5830882	A	19981103	US 1995-462615	19950605 <--
US 5852002	A	19981222	US 1995-462147	19950605 <--
US 6194392	B1	20010227	US 1995-460978	19950807
CA 2268476	AA	19980430	CA 1996-2268476	19961018 <--
WO 9817320	A1	19980430	WO 1996-CA700	19961018 <--
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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9672721	A1	19980515	AU 1996-72721	19961018 <--
AU 739701	B2	20011018		
EP 952855	A1	19991103	EP 1996-934250	19961018
EP 952855	B1	20050727		
R: DE, FR, GB, IT, SE				
NZ 335259	A	20001222	NZ 1996-335259	19961018
ZA 9608847	A	19970527	ZA 1996-8847	19961022 <--
US 6475795	B1	20021105	US 1997-860696	19970616
US 2003036525	A1	20030220	US 2002-234355	20020904

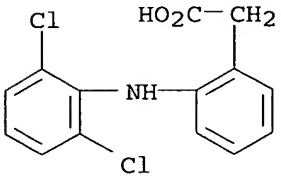
PRIORITY APPLN. INFO.:			
US 1991-675908	A2	19910703	
CA 1994-2122551	A	19940429	
WO 1995-CA243	W	19950427	
CA 1989-612307	A	19890921	
WO 1990-CA306	W	19900918	
CS 1990-4598	A	19900921	

WO 1996-CA700 A 19961018
US 1997-860696 A1 19970616

AB A method of clearing atherosclerosis comprises administering to a patient at least one dosage amount of a pharmaceutical composition comprising an effective nontoxic amount of each of a chelating agent, a nonsteroidal antiinflammatory drug (NSAID), an anti-oxidant and a form of hyaluronic acid, selected from hyaluronic acid, salts thereof, homologs, analogs, derivs., esters, complexes, fragments and subunits.

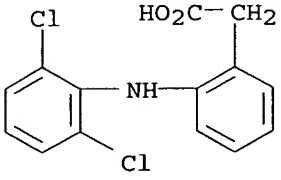
IT **15307-79-6**, Diclofenac sodium **15307-86-5**, Diclofenac **15687-27-1**, Ibuprofen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clearing of atherosclerosis with **pharmaceutical** composition containing chelating agent, NSAID, antioxidant, and hyaluronic acid or hyaluronic acid salt or derivative)

RN 15307-79-6 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)

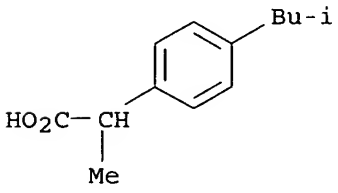


● Na

RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:621121 HCAPLUS
DOCUMENT NUMBER: 129:239916
TITLE: Therapeutic augmentation of oxyalkylene diesters and butyric acid derivatives with inhibitors of fatty acid β-oxidation
INVENTOR(S): Rephaeli, Ada
PATENT ASSIGNEE(S): Beacon Laboratories, L.L.C., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840078	A1	19980917	WO 1998-US4652	19980311 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5939455	A	19990817	US 1997-814222	19970311
AU 9865478	A1	19980929	AU 1998-65478	19980311 <--

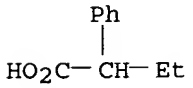
PRIORITY APPLN. INFO.:

US 1997-814222	A	19970311
WO 1998-US4652	W	19980311

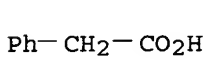
AB This invention provides a method of augmenting the therapeutic activity of an oxyalkylene-containing compound, butyric acid, a butyric acid salt or butyric acid derivative by administering an inhibitor of β-oxidation of fatty acids to a patient or to host cells. Pharmaceutical compns. are also included.

IT **90-27-7**, 2-Phenylbutyric acid **103-82-2**, Phenylacetic acid, biological studies **5104-49-4**, Flurbiprofen **15307-86-5**, Diclofenac **15687-27-1 22071-15-4**, Ketoprofen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxyalkylene diester and butyric acid derivative **therapeutic** augmentation with fatty acid β-oxidation inhibitors)

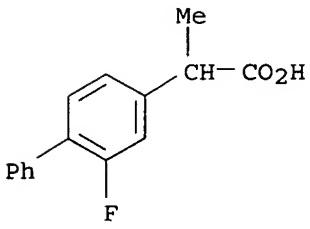
RN 90-27-7 HCAPLUS
CN Benzeneacetic acid, α-ethyl- (9CI) (CA INDEX NAME)



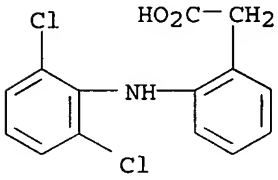
RN 103-82-2 HCAPLUS
CN Benzeneacetic acid (9CI) (CA INDEX NAME)



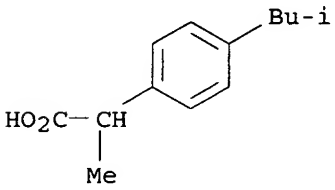
RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)



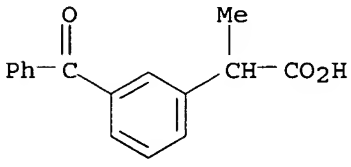
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

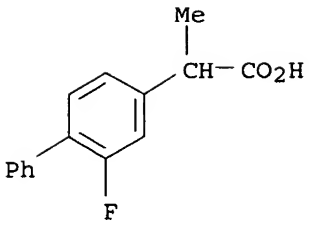
L34 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:621109 HCAPLUS
DOCUMENT NUMBER: 129:239915
TITLE: Metabolically stabilized oxyalkylene esters and therapeutic uses thereof
INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada; Neiss, Edward; Loev, Bernard
PATENT ASSIGNEE(S): Beacon Laboratories L.L.C., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840066	A1	19980917	WO 1998-US4753	19980311 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6110955	A	20000829	US 1997-814975	19970311
AU 9864579	A1	19980929	AU 1998-64579	19980311 <--
EP 986380	A1	20000322	EP 1998-910307	19980311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

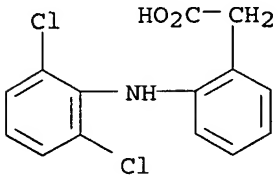
PRIORITY APPLN. INFO.: US 1997-814975 A 19970311
WO 1998-US4753 W 19980311
OTHER SOURCE(S): MARPAT 129:239915

AB Compns. for and methods of treating, preventing or ameliorating cancer and other proliferative diseases are disclosed, as are methods of inducing wound healing, treating cutaneous ulcers, treating gastrointestinal disorders, treating blood disorders such as anemias, immunomodulation, enhancing recombinant gene expression, treating insulin-dependent patients, treating cystic fibrosis patients, inhibiting telomerase activity, treating virus-associated tumors, especially EBV-associated tumors, modulating gene expression and particularly augmenting expression of a tumor suppressor gene, inducing tolerance to an antigen and treating, ameliorating or preventing protozoan infection. The methods of the invention use metabolically stabilized oxyalkylene esters.

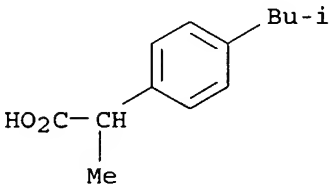
IT **5104-49-4D**, Flurbiprofen, derivs. **15307-86-5D**, Diclofenac, derivs. **15687-27-1D**, derivs. **22071-15-4D**, Ketoprofen, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolically stabilized oxyalkylene esters and **therapeutic** uses thereof)
RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)



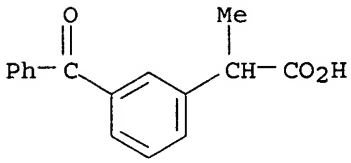
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



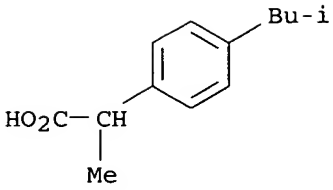
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



IT **15687-27-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; metabolically stabilized oxyalkylene esters and **therapeutic** uses thereof)
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



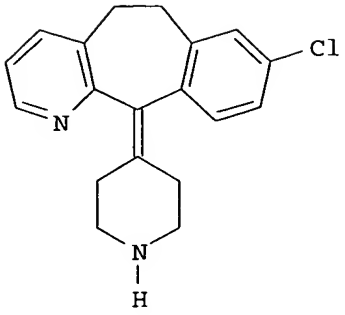
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:548533 HCAPLUS
DOCUMENT NUMBER: 129:180143
TITLE: Lactose-free, non-hygroscopic and anhydrous pharmaceutical compositions of descarboethoxyloratadine
INVENTOR(S): Redmon, Martin P.; Butler, Hal T.; Wald, Stephen A.; Rubin, Paul D.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834614	A1	19980813	WO 1998-US2328	19980206 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 522014	B	20030301	TW 1998-87101236	19980203
ZA 9800977	A	19980730	ZA 1998-977	19980206 <--
AU 9862719	A1	19980826	AU 1998-62719	19980206 <--
EP 969836	A1	20000112	EP 1998-904980	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 335041	A	20000929	NZ 1998-335041	19980206
CA 2267136	C	20001128	CA 1998-2267136	19980206
BR 9806157	A	20010109	BR 1998-6157	19980206
JP 2001511184	T2	20010807	JP 1998-534919	19980206
RU 2209627	C2	20030810	RU 1999-107283	19980206
CN 1132579	B	20031231	CN 1998-802313	19980206
EP 1614421	A2	20060111	EP 2005-108474	19980206
EP 1614421	A3	20060215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, AL, BA, HR, YU				
NO 9902157	A	19990504	NO 1999-2157	19990504 <--
US 2002123504	A1	20020905	US 2002-82685	20020225
AU 2002045909	A5	20030327	AU 2002-45909	20020611
AU 776837	B2	20040923		
US 2006079489	A1	20060413	US 2005-292695	20051202

PRIORITY APPLN. INFO.:		
US 1997-37325P	P	19970207
US 1997-45184P	P	19970430
US 1997-53050P	P	19970721
AU 1998-62719	A3	19980206
EP 1998-904980	A3	19980206
US 1998-19955	B1	19980206
WO 1998-US2328	W	19980206
US 2000-721088	B1	20001122
US 2002-82685	A1	20020225

GI

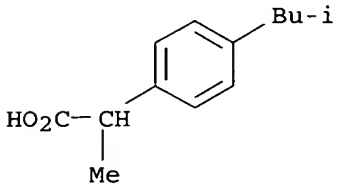


I

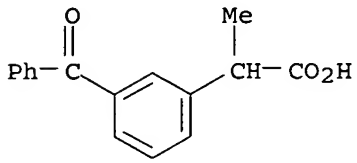
AB Stable pharmaceutical compns. of descarboethoxyloratadine (DCL) (I), a metabolic derivative of loratadine, for the treatment of allergic rhinitis and other histamine-induced disorders are disclosed. The compns. are formulated to avoid the incompatibility between I and reactive excipients such as lactose and other mono- and di-saccharides. Tablets were prepared containing I 10, starch 60, talc 12, acacia 12, and stearic acid 1 mg/tablet.

IT **15687-27-1 22071-15-4**, Ketoprofen
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactose-free, non-hygroscopic and anhydrous **pharmaceutical** compns. of descarboethoxyloratadine)

RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



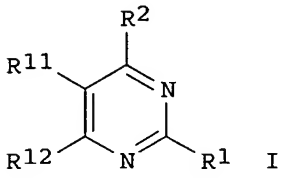
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:394334 HCAPLUS
DOCUMENT NUMBER: 129:67791
TITLE: Preparation of 2-substituted 5-(4-fluorophenyl)-4-(4-pyridyl)pyrimidines and related compounds as drugs
INVENTOR(S): Spohr, Ulrike D.; Malone, Michael J.; Mantlo, Nathan B.
PATENT ASSIGNEE(S): Amgen Inc., USA; Spohr, Ulrike D.; Malone, Michael J.; Mantlo, Nathan B.
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824782	A2	19980611	WO 1997-US22390	19971204 <--
WO 9824782	A3	19980827		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9710727	A	19980612	ZA 1997-10727	19971128 <--
CA 2274063	AA	19980611	CA 1997-2274063	19971204 <--
AU 9860120	A1	19980629	AU 1998-60120	19971204 <--
AU 733877	B2	20010531		
EP 948497	A2	19991013	EP 1997-954778	19971204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9713850	A	20000229	BR 1997-13850	19971204
CN 1246858	A	20000308	CN 1997-181563	19971204
NZ 335997	A	20010831	NZ 1997-335997	19971204
JP 2002514195	T2	20020514	JP 1998-525850	19971204
TW 520362	B	20030211	TW 1997-86118244	19971204
EP 1314731	A2	20030528	EP 2002-27704	19971204
EP 1314731	A3	20040102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, RO, MK, AL				
EP 1314732	A2	20030528	EP 2002-27705	19971204
EP 1314732	A3	20040102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, AL				
ZA 9710911	A	19980605	ZA 1997-10911	19971205 <--
MX 9905168	A	20000228	MX 1999-5168	19990603
US 6410729	B1	20020625	US 2000-598740	20000621
US 2003069425	A1	20030410	US 2002-117552	20020403
US 6610698	B2	20030826		

PRIORITY APPLN. INFO.:		
US 1996-32128P	P	19961205
US 1997-50950P	P	19970613
US 1997-976054	A	19971121
EP 1997-954778	A3	19971204
US 1997-984774	B1	19971204
WO 1997-US22390	W	19971204
US 2000-598740	A3	20000621

OTHER SOURCE(S): MARPAT 129:67791
GI

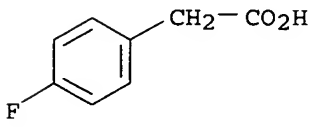


I

AB Novel pyrimidines [I; R1, R2 = ZY, with a proviso; Z = bond, (un)substituted alk(en)yl, alkynyl, (un)substituted heterocyclyl, (un)substituted (hetero)aryl; etc; Y = H, halo, NO2, COR20, CNR5NR5R21, OR21, O2CR21, etc.; R5 = H, (un)substituted alk(en)yl, alkynyl, cycloalkyl, (hetero)aryl, etc.; R20 = (un)substituted alk(en)yl, alkynyl, aralkoxy, aralkylthio, aralkylsulfonyl, etc.; R21 = H, any of definitions for R20] and their pharmaceutically acceptable salts, effective for prophylaxis and treatment of diseases mediated by tumor necrosis factor α (TNF-α), IL-1β, IL-6 and/or IL-8 and other maladies, e.g., pain and **diabetes**, were prepared, e.g., by enamination of 2-(4-fluorophenyl)-1-(4-pyridinyl)ethanone (II) with (Me2N)2CHOMe and cyclocondensation of the resulting (dimethylamino)propenone with an amidine, guanidine or urea. I analogs, prodrugs , pharmaceutical compns., methods for prophylaxis and treatment of diseases or conditions involving inflammation, pain, **diabetes**, etc., and processes for making such compds. and their intermediates are also claimed. For example, heating a mixture of II with (Me2N)2CHOMe at 110° for 1.5 h under Ar gave 3-(dimethylamino)-2-(4-fluorophenyl)-1-(4-pyridyl)-3-propen-1-one which was cyclocondensed with 4-pyridylamidine (prepared in situ from pyridylamidine-HCl and Na) by refluxing in EtOH to give a title compound I (R1 = R12 = 4-pyridinyl, R2 = H, R11 = 4-FC6H4). The latter in mice inhibited lipopolysaccharide-induced TNF-α release with IC50 ≤20 μM.

IT **405-50-5**, 4-Fluorophenylacetic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation with pyridinecarboxaldehyde; preparation of 2-substituted (fluorophenyl)(pyridyl)pyrimidines and related compds. as **drugs**)

RN 405-50-5 HCAPLUS
CN Benzeneacetic acid, 4-fluoro- (9CI) (CA INDEX NAME)



L34 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:79365 HCAPLUS
DOCUMENT NUMBER: 128:145364
TITLE: Pharmaceutical suspensions containing substantially water-insoluble drugs
INVENTOR(S): Koch, Edward A.
PATENT ASSIGNEE(S): Alpharma USPD, Inc., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

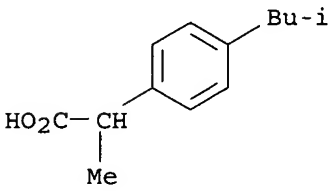
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5712310	A	19980127	US 1996-664338	19960614 <--

PRIORITY APPLN. INFO.: US 1996-664338 19960614

AB A stable aqueous suspension contained a substantially water-insol. drug suspended in a completely water-soluble mixture including hydroxypropylmethyl cellulose, polyoxyethylene sorbitan monooleate, and xanthan gum. A suspension contained HPMC 6.00, xanthan gum 1.80, Polysorbate-80 1, sodium benzoate 2, anhydrous citric acid 2, ibuprofen 20, FD&C Red #40 0.0100, D&C Yellow #10 0.0250, flavors 0.6. g, glycerin (96%) 80, sucrose syrup #2 333, and deionized water q.s. 1000 mL.

IT **15687-27-1**, Ibuprofen.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** suspensions containing substantially water-insol. **drugs**)

RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



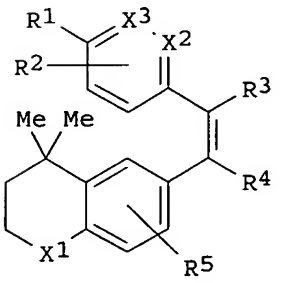
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:499165 HCAPLUS
DOCUMENT NUMBER: 127:176578
TITLE: Preparation of aromatic polycyclic retinoid-type derivatives for making pharmaceutical and cosmetic compositions
INVENTOR(S): Leblond, Bertrand; Darro, Francis; Deyine, Abdallah; Sales-Sallans, Veronique; Duhamel, Pierre; Kiss, Robert; Schoofs, Alain-Rene; Germain, Pierre; Pourrias, Bertrand; et al.
PATENT ASSIGNEE(S): Centre Europeen de Bioprospective - Ceb, Fr.
SOURCE: PCT Int. Appl., 192 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

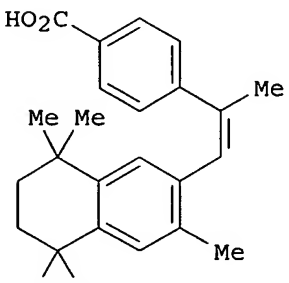
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9726237	A1	19970724	WO 1997-FR79	19970116 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2743560	A1	19970718	FR 1996-497	19960117 <--
FR 2743560	B1	19980403		
CA 2243295	AA	19970724	CA 1997-2243295	19970116 <--
AU 9713145	A1	19970811	AU 1997-13145	19970116 <--
EP 879223	A1	19981125	EP 1997-900659	19970116 <--
EP 879223	B1	20011107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000507208	T2	20000613	JP 1997-525493	19970116
AT 208365	E	20011115	AT 1997-900659	19970116
US 6265423	B1	20010724	US 1998-119066	19980715

PRIORITY APPLN. INFO.: FR 1996-497 A 19960117
WO 1997-FR79 W 19970116

OTHER SOURCE(S): MARPAT 127:176578
GI



I



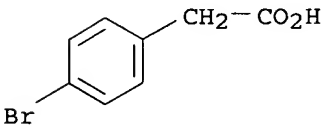
II

AB Polycyclic retinoid analogs I [X1 = CMe2, SO, SO2; X2 = X3 = CH, O, NH, S, bond; R1 = hydroxymethyl, OH, CHO, carboxyl, acyloxymethyl, SH, alkylthio, PO3H2, carbamoyl, tetrazolyl; R2 = H, F, carboxy, alkyl, haloalkyl; R3 = H, CF3, F, alkyl, arylalkyl, alkyloxy, acyl; R4 = H, aryl; R5 = H, halogen, alkyl, arylalkyl, fluoroalkyl; R5 = H, Me, Et] were prepared for a variety of pharmaceutical and cosmetic uses including anticancer agents, non-insulin dependent **diabetes** agents, anti-inflammatories, and treatments for skin disorders. Thus, retinoid analog II, as well as the corresponding E-isomer, were prepared starting from 2,5-dimethyl-2,5-hexanediol and 4-cyanoacetophenone and were tested against ZR-75-1 and T-47D cancer cell lines for antitumor activity. Structure activity relationships for antitumor activity for analogs I was also presented.

IT **1878-68-8**, 2-(4-Bromophenyl)acetic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aromatic polycyclic retinoid-type derivs. for making **pharmaceutical** and cosmetic compns.)

RN 1878-68-8 HCAPLUS

CN Benzeneacetic acid, 4-bromo- (9CI) (CA INDEX NAME)



L34 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:347295 HCAPLUS
DOCUMENT NUMBER: 126:321093
TITLE: Preparation of drug nanoparticles by spray drying
INVENTOR(S): Selvaraj, Ulagaraj; Messing, Gary L.
PATENT ASSIGNEE(S): Penn State Research Foundation, USA; Selvaraj, Ulagaraj; Messing, Gary L.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

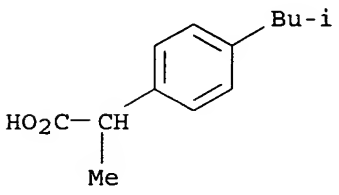
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713503	A1	19970417	WO 1996-US16417	19961011 <--
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 862420	A1	19980909	EP 1996-939455	19961011 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1995-5194P P 19951013
WO 1996-US16417 W 19961011

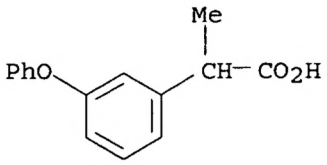
AB The present invention relates to a method for manufacturing nanoparticles comprising combining an agent and a matrix to form a composite mixture and spray drying the composite mixture, wherein the nanoparticles are less than about 5000 nm. Suitable agents that can be formulated into nanoparticle include therapeutic and diagnostic agents, cosmetics, dyes, photog. agent, foods, pesticides, among others. Et 3,5-diacetamido-2,4,6-triiodobenzoate 5 g was dissolved in 100 mL DMSO and to this solution, 10 g sucrose dissolved in 10 mL water was added. The solution was sonicated and then atomized. The atomized droplets were transported through the glass tubing at 60-250° to obtain fine particulates.

IT **15687-27-1**, Ibuprofen **29679-58-1**, Fenoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix material for preparation of **drug** nanoparticles by spray drying)

RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 29679-58-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-3-phenoxy- (9CI) (CA INDEX NAME)


Me
PhO
CH
CO2H

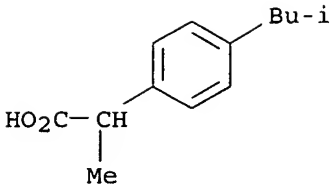
L34 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:710532 HCAPLUS
DOCUMENT NUMBER: 125:339050
TITLE: Pharmaceutical composition containing sucralfate and active ingredients in separate compartments to improve bioavailability
INVENTOR(S): Higo, Shoichi; Igusa, Kazuo
PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9631218	A1	19961010	WO 1996-JP891	19960402 <--
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, KE, KG, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 08333259	A2	19961217	JP 1996-79097	19960401 <--
CA 2217233	AA	19961010	CA 1996-2217233	19960402 <--
AU 9651233	A1	19961023	AU 1996-51233	19960402 <--
EP 823255	A1	19980211	EP 1996-907749	19960402 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1183044	A	19980527	CN 1996-193604	19960402 <--
US 5985843	A	19991116	US 1997-930263	19970926
AU 746091	B2	20020418	AU 2000-11353	20000114
PRIORITY APPLN. INFO.:			JP 1995-77781 A	19950403
			WO 1996-JP891 W	19960402

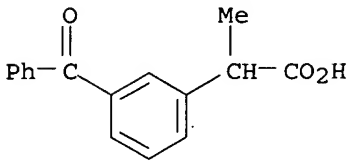
AB Disclosed herein is a pharmaceutical preparation which contains sucralfate together with another drug and consists of a delayed-release part containing sucralfate and an immediate-release part containing the other drug. When administered, this pharmaceutical preparation exerts an excellent effect of sustaining its inherent absorption characteristics, since the other drug is neither adsorbed nor trapped by sucralfate contained together therein. Delayed-release powders containing sucralfate 1000, polyethylene glycol-6000 1000, Mg stearate 2, and hydrous silica 4 g and immediate-release powders containing famotidine 10, microcryst. cellulose 300, and polyethylene glycol-6000 25 g, were compressed to give a double-layered tablet.

IT **15687-27-1**, Ibuprofen **22071-15-4**, Ketoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** composition containing sucralfate and active ingredients in sep. compartments to improve bioavailability)

RN 15687-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



L34 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:710480 HCAPLUS
DOCUMENT NUMBER: 125:339041
TITLE: Pharmaceutical composition containing film-forming polymers for transdermal delivery
PATENT ASSIGNEE(S): Sanofi, Fr.; Saunal, Henry; Illel, Brigitte
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9630000	A1	19961003	WO 1996-FR480		19960329	<--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI						
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN						
FR 2732223	A1	19961004	FR 1995-3776		19950330	<--
FR 2732223	B1	19970613				
CA 2214845	AA	19961003	CA 1996-2214845		19960329	<--
CA 2214845	C	20030107				
AU 9654022	A1	19961016	AU 1996-54022		19960329	<--
AU 704150	B2	19990415				
ZA 9602536	A	19970929	ZA 1996-2536		19960329	<--
EP 817621	A1	19980114	EP 1996-911002		19960329	<--
EP 817621	B1	20010620				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI						
CN 1182365	A	19980520	CN 1996-193453		19960329	<--
CN 1108790	B	20030521				
BR 9607862	A	19980630	BR 1996-7862		19960329	<--
JP 11502828	T2	19990309	JP 1996-529024		19960329	<--
IL 117728	A1	19990817	IL 1996-117728		19960329	
RU 2161957	C2	20010120	RU 1997-118149		19960329	
AT 202280	E	20010715	AT 1996-911002		19960329	
ES 2160239	T3	20011101	ES 1996-911002		19960329	
PT 817621	T	20011130	PT 1996-911002		19960329	
SK 282634	B6	20021008	SK 1997-1306		19960329	
CZ 291914	B6	20030618	CZ 1997-3081		19960329	
PL 186004	B1	20030930	PL 1996-322502		19960329	
TW 442296	B	20010623	TW 1996-85104149		19960409	
NO 9704507	A	19970929	NO 1997-4507		19970929	<--
US 6010716	A	20000104	US 1997-930004		19971203	
GR 3036630	T3	20011231	GR 2001-401488		20010917	
PRIORITY APPLN. INFO.:			FR 1995-3776	A	19950330	
			WO 1996-FR480	W	19960329	

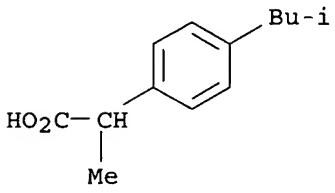
OTHER SOURCE(S): MARPAT 125:339041
AB A pharmaceutical composition for transdermal delivery comprises (a) optionally a polymeric release matrix capable of forming a flexible film when dried selected from cellulose polymers or copolymers and vinylpyrrolidone/vinyl acetate copolymers, (b) an active principle, (c) a transcutaneous absorption promoter for the active principle, and (d) a physiol. acceptable non-aqueous solvent capable of dissolving the release matrix, the active principle and the transcutaneous absorption promoter, and quickly removing same by evaporation on contact with the skin. A transdermal composition

contained Et cellulose 5, estradiol 2, 2-ethyl-hexyl-2-ethyl-hexanoate 20, and ethanol 73%.

IT **15687-27-1**, Ibuprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** composition containing film-forming polymers for transdermal delivery)

RN 15687-27-1 HCAPLUS

CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



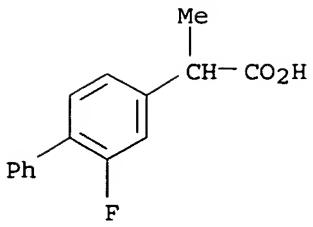
L34 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:357034 HCAPLUS
DOCUMENT NUMBER: 125:19027
TITLE: Oral pharmaceutical and/or nutritional microcapsules comprising polymer coating
INVENTOR(S): Autant, Pierre; Selles, Jean-Philippe; Soula, Gerard
PATENT ASSIGNEE(S): Flamel Technologies, Societe Anonyme, Fr.
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 709087	A1	19960501	EP 1995-420286	19951018 <--
EP 709087	B1	19991229		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2725623	A1	19960419	FR 1994-12759	19941018 <--
FR 2725623	B1	19970221		
CA 2160762	AA	19960419	CA 1995-2160762	19951017 <--
CA 2160762	C	20041221		
ZA 9508762	A	19960509	ZA 1995-8762	19951017 <--
US 6022562	A	20000208	US 1995-544208	19951017
IL 115646	A1	20000716	IL 1995-115646	19951017
WO 9611675	A2	19960425	WO 1995-FR1369	19951018 <--
WO 9611675	A3	19960620		
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9538077	A1	19960506	AU 1995-38077	19951018 <--
BR 9509286	A	19971014	BR 1995-9286	19951018 <--
JP 10509427	T2	19980914	JP 1996-513006	19951018 <--
AT 188117	E	20000115	AT 1995-420286	19951018
ES 2140641	T3	20000301	ES 1995-420286	19951018
IN 184436	A	20000826	IN 1995-DE1913	19951018
PRIORITY APPLN. INFO.:			FR 1994-12759 A	19941018
			WO 1995-FR1369 W	19951018

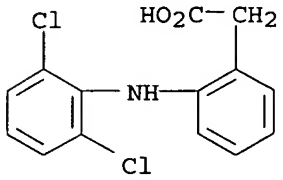
AB Microcapsules containing pharmaceutical or nutritional agents having particle size ≤1000μm and are coated with film-forming polymers are disclosed. Aciclovir 2800.6, PVP 87.1, and water 1301 g were mixed and granulated, then 300 g of microparticles thus obtained were coated with a solution containing Et cellulose 120.30, PVP 13.00, castor oil 13.00, magnesium stearate 16.26, acetone 1284.70, and isopropanol 142.70 g.

IT **5104-49-4**, Flurbiprofen **15307-86-5**, Diclofenac **15687-27-1**, Ibuprofen **22071-15-4**, Ketoprofen **29679-58-1**, Fenoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **pharmaceutical** and/or nutritional microcapsules comprising polymer coating)

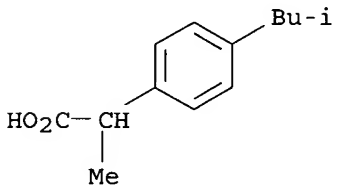
RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)



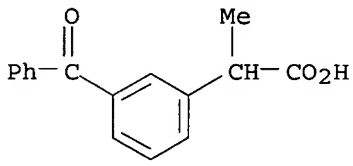
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



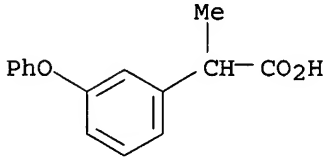
RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



RN 29679-58-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-3-phenoxy- (9CI) (CA INDEX NAME)



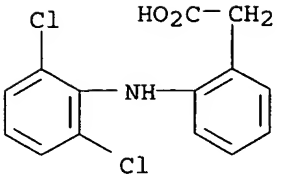
L34 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:326209 HCAPLUS
DOCUMENT NUMBER: 124:352750
TITLE: Pharmaceutical spray with systemic or local action
INVENTOR(S): Regenold, Juergen; Artmann, Carl; Roeding, Joachim
PATENT ASSIGNEE(S): Germany
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
EP 704206	A1	19960403	EP 1995-115315		19950928	<--
EP 704206	B1	20020904				
R: AT, BE, CH, DE, ES, FR, GB, GR, IE, IT, LI, NL, PT						
DE 19536244	A1	19960404	DE 1995-19536244		19950928	<--
DE 19536245	A1	19960404	DE 1995-19536245		19950928	<--
DE 19536246	A1	19960404	DE 1995-19536246		19950928	<--
CA 2201358	AA	19960411	CA 1995-2201358		19950928	<--
CA 2201358	C	20040608				
WO 9610389	A1	19960411	WO 1995-DE1351		19950928	<--
W: CA, CN, JP, KR, US						
AT 223202	E	20020915	AT 1995-115315		19950928	
PT 704206	T	20030131	PT 1995-115315		19950928	
ES 2180599	T3	20030216	ES 1995-115315		19950928	
US 5958379	A	19990928	US 1997-809384		19970527	
PRIORITY APPLN. INFO.:			DE 1994-4434995	A	19940930	
			DE 1994-4435010	A	19940930	
			WO 1995-DE1351	W	19950928	

AB A pharmaceutical liquid composition containing ≥1 systemically and/or locally acting finely divided component is applied as a spray to the skin or mucous membranes, where evaporation of the liquid phase within <4 s results in a high concentration of the active agent(s) in the residue. If the composition contains a gel-forming agent (e.g. a phospholipid mixture), the residue takes the form of a concentrated gel. This type of formulation is suitable for drugs which are usually administered orally or by injection, and can be more accurately dosed than other topical formulations such as creams and ointments; it also does not require use of excipients. Thus, a sprayable dispersion (pH 6.5) contained phospholipid gel-forming agent 10, EtOH 16, acemetacin 1, solid phosphate buffer 0.5, and H2O to 100 g.

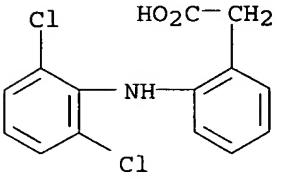
IT **15307-79-6**, Diclofenac sodium **15307-86-5**, Diclofenac **15687-27-1**, Ibuprofen **22071-15-4**, Ketoprofen **51146-56-6**, (S)-(+)-Ibuprofen **78213-16-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** spray with systemic or local action)

RN 15307-79-6 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)

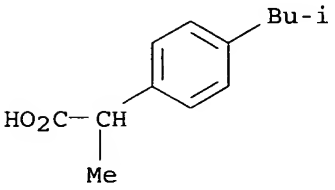


● Na

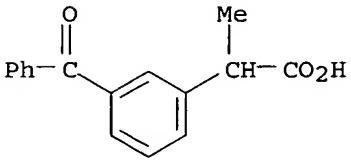
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)

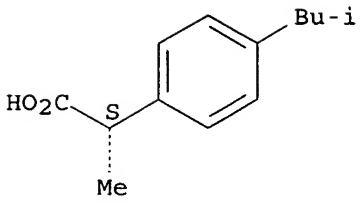


RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



RN 51146-56-6 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

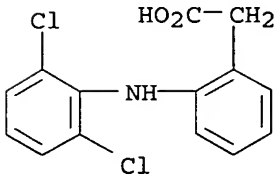
Absolute stereochemistry. Rotation (+).



RN 78213-16-8 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, compd. with N-ethylethanamine (1:1) (9CI) (CA INDEX NAME)

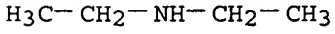
CM 1

CRN 15307-86-5
CMF C14 H11 Cl2 N O2



CM 2

CRN 109-89-7
CMF C4 H11 N



L34 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:65002 HCAPLUS
DOCUMENT NUMBER: 124:127144
TITLE: Oral pharmaceutical controlled-release liquid suspension containing oils and polymers and antioxidants
INVENTOR(S): Modi, Pankaj
PATENT ASSIGNEE(S): Can.
SOURCE: Can. Pat. Appl., 18 pp.
CODEN: CPXXEB
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

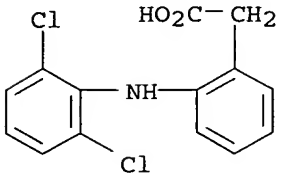
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2143070	AA	19950823	CA 1995-2143070	19950221 <--
CA 2143070	C	20011218		

PRIORITY APPLN. INFO.: US 1994-199933 A 19940222

AB A controlled-release oral formulation for use with a variety of drugs, e.g. anti-Parkinsonian, cardiovascular and anti-epileptic drugs are formed in liquid suspension form. The ingredients in the suspension are water, and edible oil and a stabilizer for the liquid suspension, at least one pharmaceutically active ingredient, at least two water soluble biodegradable polymers, and optionally with at least one antioxidant to prevent degradation and oxidation of the pharmaceutically active ingredients. A typical tsp dose of anti-Parkinson liquid suspension contains 15-150 mg carbidopa, 50-1500 mg levodopa, 100-300 mg of a combination of polyvinyl alc. and polysucrose, 10-50 mg oil, 5-15 mg antioxidant, e.g. vitamin E, 5-20 mg stabilizer, 10-15 mg colorants, 10-15 mg natural flavoring agents and 5 mL water.

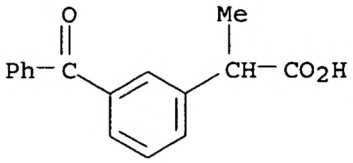
IT **15307-81-0**, Diclofenac potassium **22071-15-4**, Ketoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **pharmaceutical** controlled-release liquid suspensions containing oils and polymers and antioxidants)

RN 15307-81-0 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monopotassium salt (9CI) (CA INDEX NAME)



● K

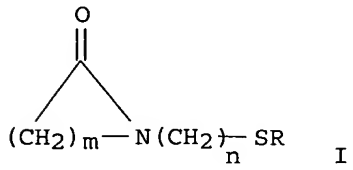
RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)


O
Me
Ph—C
CH—CO2H

L34 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:312700 HCAPLUS
DOCUMENT NUMBER: 122:114954
TITLE: Azacycloalkanes as absorption accelerators and topical preparations containing the absorption accelerators
INVENTOR(S): Tsuji, Masayoshi; Inoe, Toshitaka; Yatani, Terumi; Nakajima, Mikio; Saida, Masaru; Shimozono, Juji; Katsuki, Masumi; Sakai, Michori
PATENT ASSIGNEE(S): Hisamitsu Pharmaceutical Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06293666	A2	19941021	JP 1993-293846	19931101 <--
JP 2538513	B2	19960925		

PRIORITY APPLN. INFO.: JP 1993-293846 19931101
OTHER SOURCE(S): MARPAT 122:114954
GI

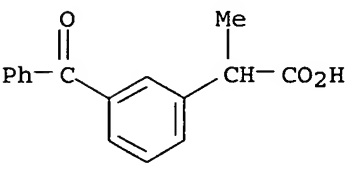


I

AB Topical prepns., useful for pharmaceuticals, cosmetics, etc., contain azacycloalkanes I (R = alkyl; m = 2-4; n = 1-15) as absorption accelerators and pharmaceuticals. A mixture of 1.11 g N-vinyl-2-pyrrolidone, 1.60 g n-nonyl mercaptan, azobisisobutyronitrile, and C6H6 were refluxed for 2-3 h to give 2.01 g 1-(2-nonylthioethyl)azacyclopentan-2-one. Solution containing ketoprofen (II) 2.8, EtOH 47.1, H2O 47.1, and I [R = (CH2)9Me, m = 3, n = 2] (III), prepared by a similar method as above, 3.0 weight% showed 77.5% permeation of II through the skin of mice in 48 h, vs. 23.4%, for control. III showed LD50 of >5 g/kg s.c. in rats.

IT **22071-15-4**, Ketoprofen
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(topical prepns. containing azacycloalkanes as absorption accelerators and **pharmaceuticals**)

RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



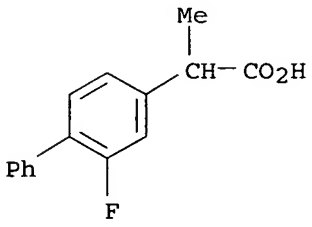
L34 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:587308 HCAPLUS
DOCUMENT NUMBER: 121:187308
TITLE: Pharmaceutical patches for transdermal administration containing penetration enhancers
INVENTOR(S): Kim, Jung Ju; Lee, Woo Young; Ahn, Jong Weon; Han, Sang Hoon
PATENT ASSIGNEE(S): Pacific Chemical Co., Ltd., S. Korea
SOURCE: Fr. Demande, 49 pp.
CODEN: FRXXBL
DOCUMENT TYPE: **Patent**
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2698787	A1	19940610	FR 1992-14836	19921209 <--
FR 2698787	B1	19960621		
KR 9606859	B1	19960523	KR 1992-3699	19920306 <--
GB 2273044	A1	19940608	GB 1992-25218	19921202 <--
GB 2273044	B2	19970409		
IN 175104	A	19950429	IN 1993-MA140	19930224 <--
JP 07258060	A2	19951009	JP 1993-44136	19930304 <--
CN 1076110	A	19930915	CN 1993-102465	19930306 <--
CN 1056509	B	20000920		
PRIORITY APPLN. INFO.:			KR 1992-3699	19920306

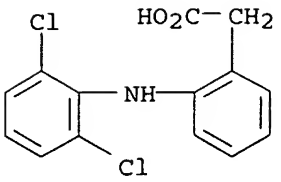
AB Pharmaceutical patches for transdermal administration contain penetration enhancers such as fatty acid esters. A transdermal patch contained ketoprofen 10, PEG monolaurate 10, tocopheryl acetate 1, ZnO 5, and Bu acrylate-vinyl octyl acetate copolymer 74%.

IT **5104-49-4**, Flurbiprofen **15307-79-6**, Sodium diclofenac **22071-15-4**, Ketoprofen
RL: BIOL (Biological study)
(transdermal **pharmaceutical** patches containing penetration enhancers and)

RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)

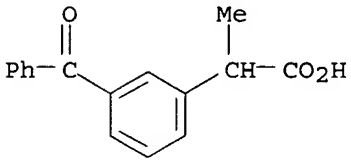


RN 15307-79-6 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



L34 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:253379 HCAPLUS
DOCUMENT NUMBER: 120:253379
TITLE: Pharmaceutical compositions containing terfenadine derivatives and their optically pure isomers for treating allergic disorders
INVENTOR(S): Young, James W.; Gray, Nancy M.; Woosley, Raymond L.; Chen, Yiwang
PATENT ASSIGNEE(S): Sepracor Inc., USA; Georgetown University
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403170	A1	19940217	WO 1993-US7260	19930803 <--
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9347986	A1	19940303	AU 1993-47986	19930803 <--
AU 675240	B2	19970130		
GB 2284351	A1	19950607	GB 1995-2183	19930803 <--
GB 2284351	B2	19961127		
JP 08500348	T2	19960116	JP 1994-505499	19930803 <--
JP 3041954	B2	20000515		
HU 71889	A2	19960228	HU 1995-313	19930803 <--
EP 701443	A1	19960320	EP 1993-918584	19930803 <--
EP 701443	B1	19980121		
EP 701443	B2	20001122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
EP 815860	A2	19980107	EP 1997-104837	19930803 <--
EP 815860	A3	19980114		
EP 815860	B1	20060412		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 162399	E	19980215	AT 1993-918584	19930803 <--
ES 2086270	T3	19980301	ES 1993-918584	19930803 <--
PL 174373	B1	19980731	PL 1993-307339	19930803 <--
BR 9306841	A	19981208	BR 1993-6841	19930803 <--
JP 2000086512	A2	20000328	JP 1999-291216	19930803
JP 2000086516	A2	20000328	JP 1999-291230	19930803
JP 3037697	B2	20000424		
RO 116043	B1	20001030	RO 1995-160	19930803
CA 2141572	C	20010206	CA 1993-2141572	19930803
RU 2167657	C2	20010527	RU 1995-107881	19930803
EP 1214937	A2	20020619	EP 2002-6356	19930803
EP 1214937	A3	20021030		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5375693	A	19941227	US 1994-191061	19940202 <--
NO 9500374	A	19950329	NO 1995-374	19950201 <--
NO 310644	B1	20010806		
FI 9500467	A	19950331	FI 1995-467	19950202 <--
AU 9671822	A1	19970130	AU 1996-71822	19961119 <--
AU 9918429	A1	19990429	AU 1999-18429	19990225 <--
JP 2000086513	A2	20000328	JP 1999-291220	19991013
JP 3288660	B2	20020604		
JP 2000086514	A2	20000328	JP 1999-291223	19991013

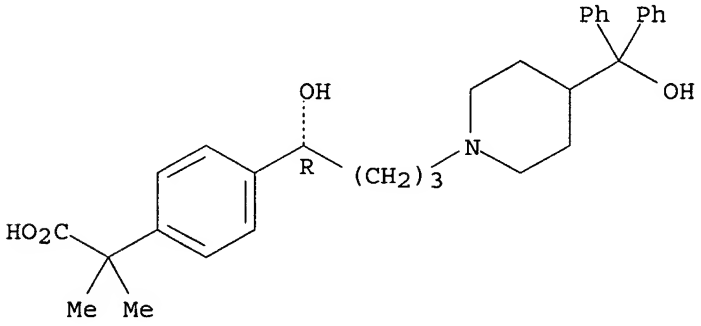
JP 3288661	B2	20020604			
JP 2000086515	A2	20000328	JP 1999-291228		19991013
JP 3288662	B2	20020604			
GR 3035417	T3	20010531	GR 2001-400247		20010214
AU 782660	B2	20050818	AU 2001-97409		20011224
AU 2005222506	A1	20051103	AU 2005-222506		20051011
PRIORITY APPLN. INFO.:			US 1992-924156	A	19920803
			US 1992-924182	A	19920803
			EP 1993-918584	A3	19930803
			EP 1997-104837	A3	19930803
			JP 1994-505499	A3	19930803
			WO 1993-US7260	W	19930803
			AU 1996-71822	A3	19961119
			AU 1999-18429	A3	19990225

AB Pharmaceutical compns. comprising terfenadine or a salt thereof (Markush structure given), are used as antihistaminic agents which do not induce any significant cardiac arrhythmia. Thus, Me S-4-[1-oxo-4-(4-hydroxydiphenylmethyl-1-piperidinyl)buyl]-α,α-dimethylbenzeneacetacetate was reduced to obtain Me S-4-[1-hydroxy-4-(4-hydroxydiphenylmethyl-1-piperidinyl)buyl]-α,α-dimethylbenzeneacetacetate (I). I was refluxed with NaOH and EtOH for 7 hs and the residue was dissolved in water and the aqueous solution was acidified with glacial AcOH to provide S-terfenadine carboxylate (II). II at 10-9 concentration inhibited the binding of pyrilamine to histamine H1 receptors by 8.1%. A capsule contained I 30.0, starch-1500 69.0, Mg stearate 1.0mg.

IT **139965-10-9P 139965-11-0P**
RL: PREP (Preparation)
(preparation of, as antihistamine, **pharmaceutical** compns. containing)

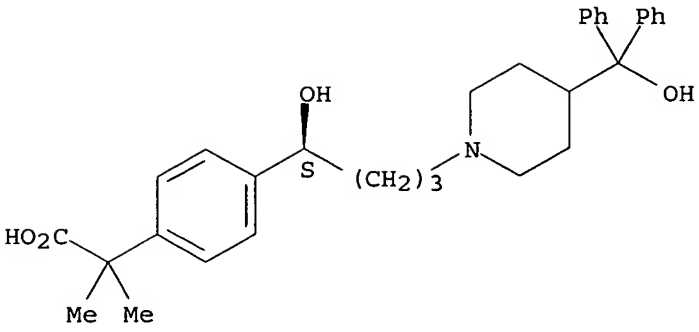
RN 139965-10-9 HCAPLUS
CN Benzeneacetic acid, 4-[(1R)-1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-α,α-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 139965-11-0 HCAPLUS
CN Benzeneacetic acid, 4-[(1S)-1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]-α,α-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).


Ph
Ph
OH
OH
S
(CH2)3
N
HO2C
Me
Me

L34 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:226984 HCAPLUS
DOCUMENT NUMBER: 120:226984
TITLE: Compositions of oral nondissolvable matrixes for transmucosal administration of medicaments
INVENTOR(S): Stanley, Theodore H.; Hague, Brian
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 20 pp. Cont.-in-part of U.S. 4,863,737.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5288498	A	19940222	US 1989-403752	19890905 <--
US 4671953	A	19870609	US 1985-729301	19850501 <--
EP 487520	A1	19920603	EP 1989-909497	19890816 <--
EP 487520	B1	19950412		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 05501539	T2	19930325	JP 1989-504878	19890816 <--
JP 2801050	B2	19980921		
AU 641127	B2	19930916	AU 1989-40704	19890816 <--
AT 120953	E	19950415	AT 1989-909497	19890816 <--
CA 1338978	A1	19970311	CA 1989-609378	19890824 <--
AU 9050352	A1	19910408	AU 1990-50352	19890905 <--
AU 645966	B2	19940203		
EP 493380	A1	19920708	EP 1990-902584	19890905 <--
EP 493380	B1	19971029		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 5132114	A	19920721	US 1989-402881	19890905 <--
JP 05501854	T2	19930408	JP 1990-502779	19890905 <--
CA 1339075	A1	19970729	CA 1989-610329	19890905 <--
AT 159658	E	19971115	AT 1990-902584	19890905 <--
CA 2066403	AA	19910306	CA 1990-2066403	19900803 <--
CA 2066403	C	19980414		
WO 9103236	A1	19910321	WO 1990-US4369	19900803 <--
W: AU, CA, JP, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9063371	A1	19910408	AU 1990-63371	19900803 <--
AU 642664	B2	19931028		
EP 490944	A1	19920624	EP 1990-913359	19900803 <--
EP 490944	B1	19960529		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05500058	T2	19930114	JP 1990-512483	19900803 <--
JP 2749198	B2	19980513		
AT 138562	E	19960615	AT 1990-913359	19900803 <--
ES 2089027	T3	19961001	ES 1990-913359	19900803 <--
NO 9200565	A	19920213	NO 1992-565	19920213 <--
NO 304056	B1	19981019		
DK 9200193	A	19920214	DK 1992-193	19920214 <--
DK 175779	B1	20050214		
NO 9200858	A	19920304	NO 1992-858	19920304 <--
NO 9200855	A	19920410	NO 1992-855	19920304 <--
NO 9200854	A	19920427	NO 1992-854	19920304 <--
DK 9200300	A	19920505	DK 1992-300	19920305 <--
DK 175773	B1	20050214		
AU 9460697	A1	19940623	AU 1994-60697	19940427 <--
US 5855908	A	19990105	US 1994-339655	19941115 <--

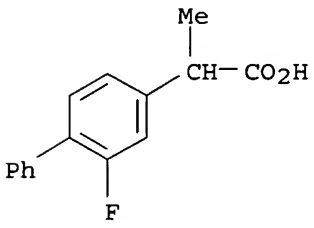
PRIORITY APPLN. INFO.:

US 1985-729301	A2	19850501
US 1987-60045	A2	19870608
EP 1989-909497	A	19890816
WO 1989-US3518	W	19890816
US 1989-403752	A	19890905
WO 1989-US3801	A	19890905
WO 1990-US4369	A	19900803
US 1993-152414	B1	19931112

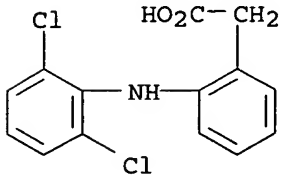
AB Compns. and methods of manufacture for producting a medicament composition capable of absorption through the mucosal tissues of the mouth, pharynx, and esophagus are disclosed. The present invention relates to such compns. and methods which are useful in administering lipophilic and nonlipophilic drugs in a dose-to-effect manner such that sufficient drug is administered to produce precisely a desired effect. The invention also relates to manufacturing techniques that enable therapeutic agents to be incorporated into nondissolvable drug containment matrixes which are capable of releasing the drug within a patient's mouth. An appliance or holder is preferably attached to the drug containment matrix. Employing the present invention the drug may be introduced into the patient's bloodstream almost as fast as through injection, and much faster than using the oral administration route, while avoiding the neg. aspects of both of these methods. The nondissolvable drug containment matrix may include permeation enhancers to increase the drug adsorption by the mucosal tissues of the mouth. The matrix composition may also include pH buffering agents to modify the saliva pH thereby increasing the absorption of the drug through the mucosal tissues. Figures show views of some dosage forms.

IT **5104-49-4**, Flurbiprofen **15307-86-5**, Diclofenac **15687-27-1**, Ibuprofen **22071-15-4**, Ketoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmucosal **pharmaceuticals** containing)

RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)

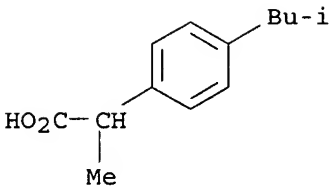


RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

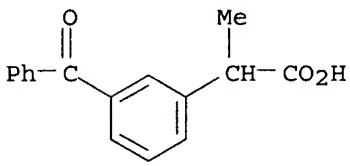


RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX

NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



L34 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:226981 HCAPLUS
DOCUMENT NUMBER: 120:226981
TITLE: Compositions of oral dissolvable medicaments
INVENTOR(S): Stanley, Theodore H.; Hague, Brian
PATENT ASSIGNEE(S): University of Utah, USA
SOURCE: U.S., 22 pp. Cont.-in-part of U.S. 4,863,737.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5288497	A	19940222	US 1989-403751	19890905 <--
US 4671953	A	19870609	US 1985-729301	19850501 <--
EP 487520	A1	19920603	EP 1989-909497	19890816 <--
EP 487520	B1	19950412		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 05501539	T2	19930325	JP 1989-504878	19890816 <--
JP 2801050	B2	19980921		
AU 641127	B2	19930916	AU 1989-40704	19890816 <--
AT 120953	E	19950415	AT 1989-909497	19890816 <--
CA 1338978	A1	19970311	CA 1989-609378	19890824 <--
AU 9050352	A1	19910408	AU 1990-50352	19890905 <--
AU 645966	B2	19940203		
EP 493380	A1	19920708	EP 1990-902584	19890905 <--
EP 493380	B1	19971029		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 5132114	A	19920721	US 1989-402881	19890905 <--
JP 05501854	T2	19930408	JP 1990-502779	19890905 <--
CA 1339075	A1	19970729	CA 1989-610329	19890905 <--
AT 159658	E	19971115	AT 1990-902584	19890905 <--
CA 2066423	AA	19910306	CA 1990-2066423	19900803 <--
CA 2066423	C	19980414		
WO 9103237	A1	19910321	WO 1990-US4384	19900803 <--
W: AU, CA, JP, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9062877	A1	19910408	AU 1990-62877	19900803 <--
AU 645265	B2	19940113		
EP 490916	A1	19920624	EP 1990-912733	19900803 <--
EP 490916	B1	19951018		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05503917	T2	19930624	JP 1990-512229	19900803 <--
EP 630647	A1	19941228	EP 1994-111352	19900803 <--
EP 630647	B1	19990303		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
AT 129148	E	19951115	AT 1990-912733	19900803 <--
ES 2077686	T3	19951201	ES 1990-912733	19900803 <--
AT 177007	E	19990315	AT 1994-111352	19900803 <--
ES 2133448	T3	19990916	ES 1994-111352	19900803
NO 9200565	A	19920213	NO 1992-565	19920213 <--
NO 304056	B1	19981019		
DK 9200193	A	19920214	DK 1992-193	19920214 <--
DK 175779	B1	20050214		
NO 9200857	A	19920406	NO 1992-857	19920304 <--
NO 304348	B1	19981207		
NO 9200855	A	19920410	NO 1992-855	19920304 <--
NO 9200854	A	19920427	NO 1992-854	19920304 <--

DK 9200300	A	19920505	DK 1992-300	19920305 <--
DK 175773	B1	20050214		
AU 9455218	A1	19940428	AU 1994-55218	19940218 <--
AU 668004	B2	19960418		
AU 9460697	A1	19940623	AU 1994-60697	19940427 <--
US 5824334	A	19981020	US 1996-636828	19960419 <--
US 5783207	A	19980721	US 1997-795359	19970204 <--
US 5785989	A	19980728	US 1997-822560	19970319 <--

PRIORITY APPLN. INFO.:

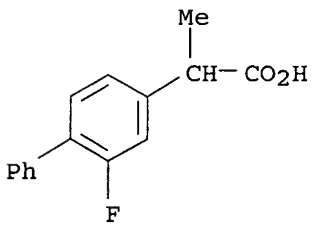
US 1985-729301	A2	19850501
US 1987-60045	A2	19870608
EP 1989-909497	A	19890816
WO 1989-US3518	W	19890816
US 1989-403751	A	19890905
WO 1989-US3801	A	19890905
EP 1990-912733	A3	19900803
WO 1990-US4384	A	19900803
US 1993-152396	B1	19931112
US 1994-333233	B2	19941102
US 1995-439127	B1	19950511

AB Compns. and methods of manufacture for producing a medicament composition capable of absorption through the mucosal tissues of the mouth, pharynx, and esophagus are disclosed. The present invention relates to such compns. and methods which are useful in administering lipophilic and nonlipophilic drugs in a dose-to-effect manner that sufficient drug is administered to produce precisely a desired effect. The invention also relates to a manufacturing technique that enables a therapeutic agent or drug to be incorporated into a flavored dissolvable matrix. An appliance or holder is preferably attached to the dissolvable matrix. Employing the present invention the drug may be introduced into the patient's bloodstream almost as fast as through injection, and much faster than using the oral administration route, while avoiding the neg. aspects of both of these methods. The present invention achieves these advantages by incorporating the drug into a carbohydrate, fat, protein, wax, or other dissolvable matrix composition The dissolvable matrix may include permeation enhancers to increase the drug absorption by the mucosal tissues of the mouth. The matrix composition may also include pH buffering agents to modify the salival pH thereby increasing the absorption of the drug through the mucosal tissue. Methohexital sodium was incorporated into a dissolvable matrix including citric acid; ribotide; Compritol 888; aspartame; vanilla, wild cherry, and peppermint microcapsules; compressible sugar; and maltodextrin.

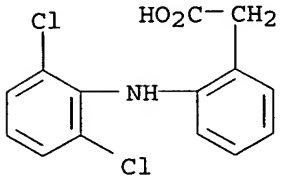
IT **5104-49-4**, Flurbiprofen **15307-86-5**, Diclofenac **15687-27-1**, Ibuprofen **22071-15-4**, Ketoprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmucosal **pharmaceuticals** containing)

RN 5104-49-4 HCAPLUS

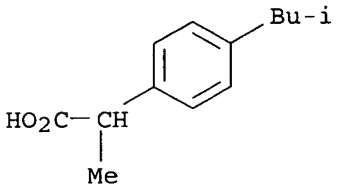
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)



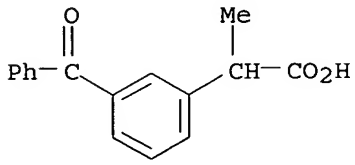
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



RN 22071-15-4 HCAPLUS
CN Benzeneacetic acid, 3-benzoyl-α-methyl- (9CI) (CA INDEX NAME)



L34 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:116847 HCAPLUS
DOCUMENT NUMBER: 120:116847
TITLE: Biodegradable controlled release melt-spun delivery system
INVENTOR(S): Fuisz, Richard C.
PATENT ASSIGNEE(S): Fuisz Technologies, Ltd., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

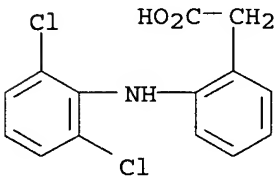
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324154	A1	19931209	WO 1993-US5307	19930602 <--
W: AU, CA, HU, JP, KR, PL, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5518730	A	19960521	US 1992-893238	19920603 <--
AU 9344058	A1	19931230	AU 1993-44058	19930602 <--
AU 665844	B2	19960118		
JP 07507548	T2	19950824	JP 1994-500877	19930602 <--
EP 746342	A1	19961211	EP 1993-914373	19930602 <--
EP 746342	B1	20020814		
R: BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				

PRIORITY APPLN. INFO.: US 1992-893238 A2 19920603
WO 1993-US5307 A 19930602

AB Biodegradable controlled-release delivery systems using melt-spun biodegradable polymers as carriers for bio-effecting agents such as pharmaceutical actives are disclosed. Oral dose forms as well as implants are described. For example, polyglycolide was melt-spun in combination with various drugs such as vancomycin, gentamicin, tolmetin, diphenhydramine, ibuprofen, and insulin and controlled drug release was demonstrated.

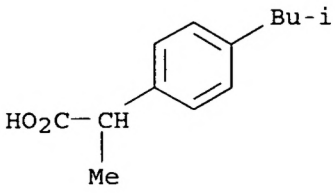
IT **15307-79-6**, Diclofenac sodium **15687-27-1**, Ibuprofen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release **pharmaceuticals** formed by flash-flow melt-spinning containing, biodegradable polymers as carriers in)

RN 15307-79-6 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)

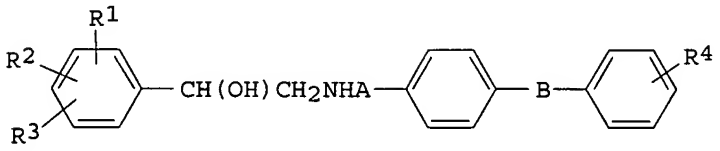

Bu-i
HO2C— CH
Me

L34 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:477643 HCAPLUS
DOCUMENT NUMBER: 111:77643
TITLE: Preparation of new phenylethanolamines and pharmaceuticals containing them
INVENTOR(S): Hurnaus, Rudolf; Reiffen, Manfred; Sauter, Robert; Grell, Wolfgang; Rupprecht, Eckhard
PATENT ASSIGNEE(S): Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3718638	A1	19881222	DE 1987-3718638	19870604 <--
WO 9006299	A1	19900614	WO 1988-EP1083	19881129 <--
W: AU, DK, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8826115	A1	19900626	AU 1988-26115	19881129 <--
AU 617139	B2	19911121		
EP 375791	A1	19900704	EP 1988-119850	19881129 <--
R: ES, GR				
EP 400011	A1	19901205	EP 1989-900024	19881129 <--
EP 400011	B1	19940126		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03503405	T2	19910801	JP 1989-500051	19881129 <--
AT 100792	E	19940215	AT 1989-900024	19881129 <--
CA 1325210	A1	19931214	CA 1988-584935	19881202 <--
DK 9001619	A	19900705	DK 1990-1619	19900705 <--
US 5232946	A	19930803	US 1990-572969	19900820 <--

PRIORITY APPLN. INFO.:
DE 1987-3718638 19870604
EP 1989-900024 A 19881129
WO 1988-EP1083 A 19881129

OTHER SOURCE(S): CASREACT 111:77643; MARPAT 111:77643
GI



I

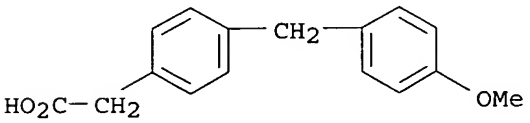
AB The title compds. [I; A = C1-5 alkylene; B = bond, C1-2 alkylene, CO, CHOH; R1 = H, halo, CF3; R2 = H, NH2; R3 = H, cyano, Cl, Br; R4 = H, halo, alkyl, OH, (un)substituted alkoxy, etc.], their optical isomers, diastereomers, and salts, useful in treatment of **diabetes** mellitus, obesity, and for treatment and prophylaxis of atherosclerosis, were prepared by 7 methods. 4-PhC6H4CO2Et in CH2Cl2 was treated with AlCl3 and MeCHClCOCl in CH2Cl2 at 0° and kept overnight at room temperature to give 4-(4-MeCHClCOC6H4)C6H4CO2Et which was refluxed 2 days with KOAc in Me2CO to give 4-[4-AcOCHMeCOC6H4]C6H4CO2Et. NaBH4 reduction and heating with polyphosphoric acid at 80° gave 4-(4-MeCOCH2C6H4)C6H4CO2Et which was treated with 3-ClC6H4CH(OH)CH2NH2 in EtOH containing NaBH3CN and AcOH at room temperature to give I (R1 = 3-Cl, R2 = R3 = H, A = CHMeCH2, B = bond, R4 =

4-CO2Et) (II). In mice 1 and 3 mg II/kg orally decreased **blood sugar** 37% and 49%, resp., vs. a control. A formulation for dragees comprised I (R1 = 3-Cl, R2 = R3 = H, A = CHMeCH2, B = CH2, R4 = 2-CO2Et) 10.0, lactose 69.0, corn starch 35.0, polyvinylpyrrolidone 5.0, and Mg stearate 1.0 mg.

IT **121805-14-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in synthesis of phenylethanolamine **pharmaceutical**)

RN 121805-14-9 HCAPLUS

CN Benzeneacetic acid, 4-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



L34 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:541114 HCAPLUS
DOCUMENT NUMBER: 107:141114
TITLE: Therapeutic formulations with bimodal release characteristics
INVENTOR(S): Shah, Ashok C.
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

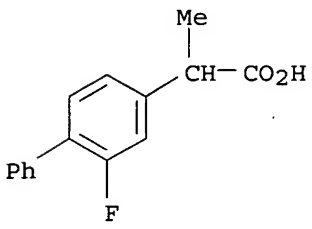
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8700044	A1	19870115	WO 1986-US1360	19860618 <--
W: JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
EP 227814	A1	19870708	EP 1986-904573	19860618 <--
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				

PRIORITY APPLN. INFO.: US 1985-751125 A2 19850702

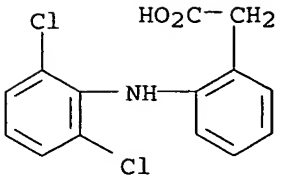
AB Sustained release pharmaceuticals with bimodal release profiles are made of medicaments combined with a carrier base of ≥1 hydroxypropylmethylcelluloses and ≤50% of methylcellulose, Na carboxymethylcellulse and/or other cellulose ethers. At least one of the hydroxypropylmethylcelluloses is bimodal, with a methoxy content of 19-30%, an hydroxypropyl content of 4-12%, and an average mol. weight of 20,000-140,000. Tablets containing flurbiprofen 58.0, metolose 65SH-4000 40.0, stearic acid 1.70 and cab-o-sil 0.34 weight % were formed. The percent of tablet (initial weight) dissolved/h was 6.10 after 1 h, between 2.70-2.90 from 2-11 h, and increased from 3.30 to 6.30 from 12-19 h.

IT **5104-49-4 15307-86-5**, Diclofenac **15687-27-1**, Ibuprofen
RL: BIOL (Biological study)
(bimodal sustained-release **pharmaceutical** containing hydroxypropyl Me cellulose and)

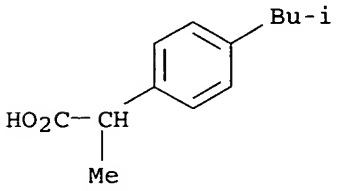
RN 5104-49-4 HCAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl- (9CI) (CA INDEX NAME)



RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



RN 15687-27-1 HCAPLUS
CN Benzeneacetic acid, α-methyl-4-(2-methylpropyl)- (9CI) (CA INDEX NAME)



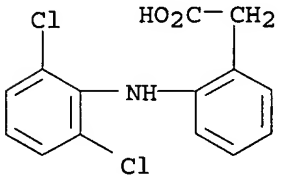
L34 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:412126 HCAPLUS
DOCUMENT NUMBER: 105:12126
TITLE: Pharmaceutical pellet preparation
INVENTOR(S): Dell, Hans Dieter; Kraus, Reinhold; Schierstedt, Detlef
PATENT ASSIGNEE(S): Troponwerke G.m.b.H. und Co. K.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3431861	A1	19860313	DE 1984-3431861	19840830 <--
CN 85102343	A	19861029	CN 1985-102343	19850401 <--
NO 8503249	A	19860303	NO 1985-3249	19850816 <--
EP 173210	A2	19860305	EP 1985-110362	19850819 <--
EP 173210	A3	19870513		
EP 173210	B1	19900516		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
AT 52688	E	19900615	AT 1985-110362	19850819 <--
AU 8546570	A1	19860306	AU 1985-46570	19850822 <--
FI 8503296	A	19860301	FI 1985-3296	19850828 <--
CA 1255223	A1	19890606	CA 1985-489611	19850828 <--
DK 8503946	A	19860301	DK 1985-3946	19850829 <--
DK 163208	B	19920210		
DK 163208	C	19920629		
ZA 8506597	A	19860430	ZA 1985-6597	19850829 <--
HU 39607	A2	19861029	HU 1985-3287	19850829 <--
JP 61065817	A2	19860404	JP 1985-190021	19850830 <--
JP 07059501	B4	19950628		
US 4900557	A	19900213	US 1988-286421	19881219 <--

PRIORITY APPLN. INFO.:
DE 1984-3431861 19840830
US 1985-765907 B3 19850814
EP 1985-110362 A 19850819
US 1986-919744 B1 19861016

AB Pellet prepns. contain at least 1 active ingredient, 1 binder, and 1 loading material and are coated with a gastric juice-resistant lacquer. They have an apparent d. of 1.4-2.4 and diameter of 0.2-1.8 mm. Thus, pellets were manufactured containing acemetacin 60, TiO2 94, Kollidon 25 13.6, cellulose acetate phthalate 20.5, talc 1.0, and triacetin 4.6 part.

IT **15307-86-5**
RL: BIOL (Biological study)
(**pharmaceutical** pellets containing)
RN 15307-86-5 HCAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

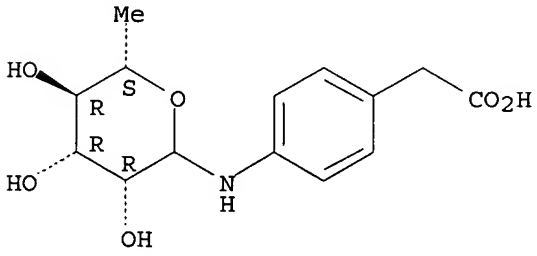


L34 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:85933 HCAPLUS
DOCUMENT NUMBER: 96:85933
TITLE: Phenylamino saccharide derivatives and pharmaceutical compositions containing them
INVENTOR(S): Yoshikumi, Chikao; Hirose, Fumio; Ohmura, Yoshio; Fujii, Takayoshi; Ikuzawa, Masanori; Ohhara, Minoru; Matsunaga, Kenichi; Ando, Takao
PATENT ASSIGNEE(S): Kureha Chemical Industry Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 38195	A1	19811021	EP 1981-301593	19810410 <--
EP 38195	B1	19841003		
R: BE, CH, DE, FR, GB, IT, SE				
JP 56145298	A2	19811111	JP 1980-47654	19800411 <--
JP 60008000	B4	19850228		
US 4372948	A	19830208	US 1981-247521	19810325 <--
ZA 8102088	A	19820428	ZA 1981-2088	19810327 <--
AU 8169078	A1	19811015	AU 1981-69078	19810403 <--
AU 534878	B2	19840216		

PRIORITY APPLN. INFO.: JP 1980-47654 A 19800411
OTHER SOURCE(S): MARPAT 96:85933
AB RC6H4NHR1 [R = CO2R2 (R2 = Ph, cyclohexyl, PhCH2, cyclohexylmethyl), CONH2, CH2CO2R3 (R3 = H, C1-4 alkyl); R1 = glycosyl from mono-, di-, or trisaccharide], with bactericidal, fungicidal, **antidiabetic**, antihypertensive, hypolipemic, analgesic, activities (extensive data given), were prepared Thus, a mixture of 2.3 g o-H2NC6H4CONH2, 2.7 g D-fructose, EtOH, and concentrated HCl was heated to give 44% o-aminobenzamide N-D-fructoside.
IT **80788-98-3P 80788-99-4P 80789-00-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and **pharmacol.** activity of)
RN 80788-98-3 HCAPLUS
CN Benzeneacetic acid, 4-[(6-deoxy-L-mannopyranosyl)amino]- (9CI) (CA INDEX NAME)

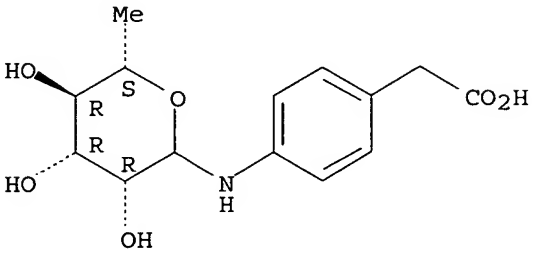
Absolute stereochemistry.



RN 80788-99-4 HCAPLUS
CN Benzeneacetic acid, 4-[(6-deoxy-L-mannopyranosyl)amino]-, monosodium salt

(9CI) (CA INDEX NAME)

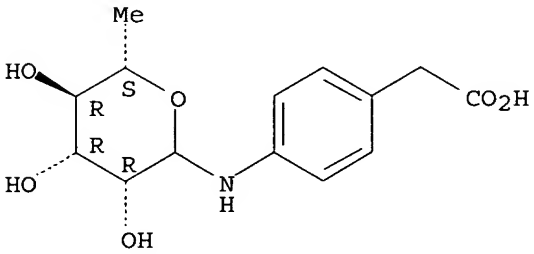
Absolute stereochemistry.



● Na

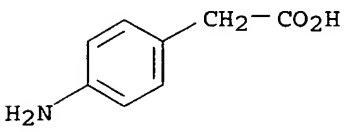
RN 80789-00-0 HCAPLUS
CN Benzeneacetic acid, 4-[(6-deoxy-L-mannopyranosyl)amino]-, monopotassium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● K

IT **1197-55-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with sugars)
RN 1197-55-3 HCAPLUS
CN Benzeneacetic acid, 4-amino- (9CI) (CA INDEX NAME)



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L1                STR
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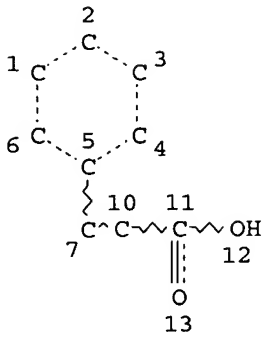


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NODE ATTRIBUTES:
NSPEC   IS RC     AT   7
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   5
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
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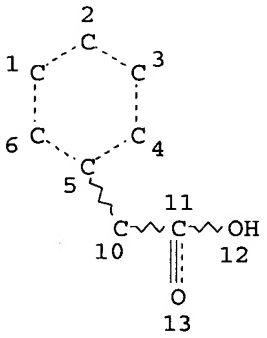


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   5
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
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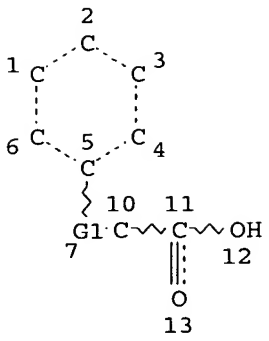
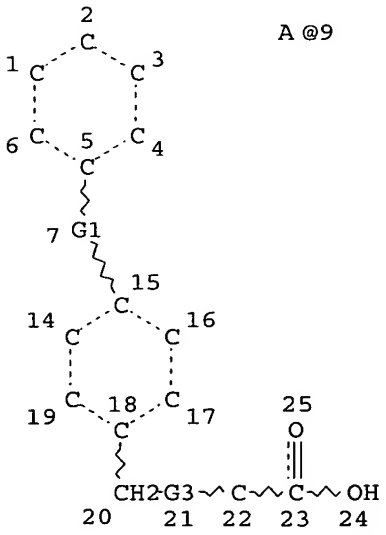


VAR G1=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 5
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L5 STR



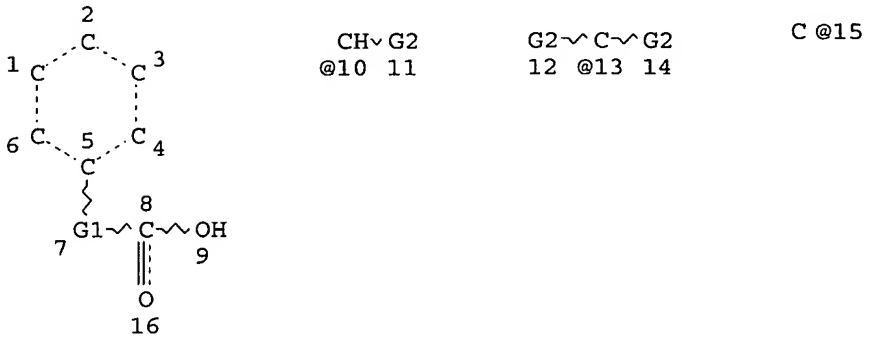
REP G1=(0-1) 9
VAR G3=O/S/N
NODE ATTRIBUTES:
NSPEC IS RC AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 14 5
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L6 105668 SEA FILE=REGISTRY SSS FUL L3 OR L4 OR L5

L14 204237 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DIABETES MELLITUS"/CV OR DIABETES/CV) OR "ANTIDIABETIC AGENTS"/CV OR HYPERGLYCEMIA/CV OR ?DIABET? OR ?HYPERGLYCEM? OR (BLD OR BLOOD)(2A)(SUGAR OR GLUCOSE) OR MUSCULAR DYSTROPHY/CV OR DYSTROPHY/CV OR MYODYSTROPHY/CV OR ?DYSTROPHY? OR ?SCLEROS?(2A)SYSTEM?

L19 STR

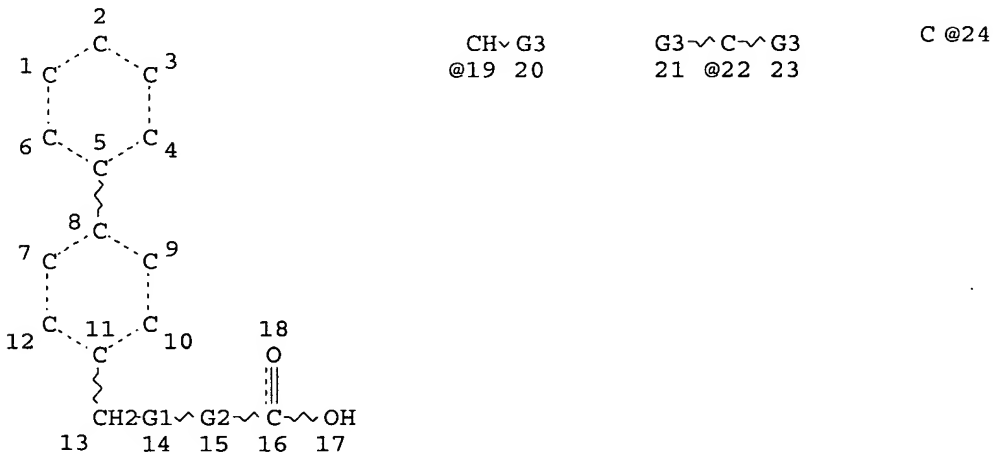


VAR G1=CH2/10/13/15
VAR G2=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L20 STR

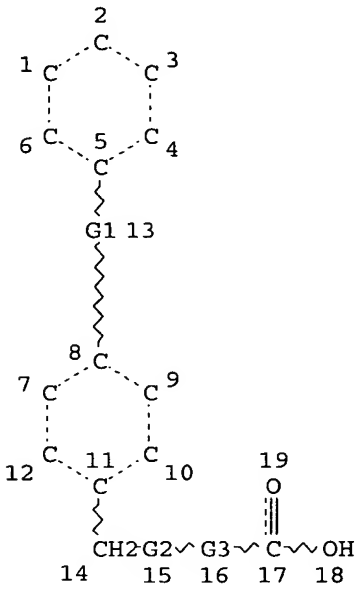


VAR G1=O/S/NH/SO2
VAR G2=CH2/19/22/24
VAR G3=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L21 STR



CH G4 @20 21
G4 C G4 22 @23 24
C @25

VAR G1=O/S/SO2/CH2/20/23/25
VAR G2=O/S/NH/SO2
VAR G3=CH2/20/23/25
VAR G4=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
L22 288559 SEA FILE=REGISTRY ABB=ON PLU=ON L2 OR L6
L24 27972 SEA FILE=REGISTRY SUB=L22 SSS FUL L19 OR L20 OR L21
L25 58477 SEA FILE=HCAPLUS ABB=ON PLU=ON L24
L26 283 SEA FILE=HCAPLUS ABB=ON PLU=ON L14(L)L25
L27 114 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND PD=<MAY 28, 1999
L28 7507 SEA FILE=HCAPLUS ABB=ON PLU=ON L25(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR ?PHARMA?)
L29 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L28
L30 1470 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L25
L31 389 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND PD=<MAY 28, 1999
L32 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND L31
L33 48 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 NOT L29
L34 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L33 AND PATENT/DT
L35 66 SEA FILE=HCAPLUS ABB=ON PLU=ON ("BILLINGHAM E J JR"/AU OR "BILLINGHAM EDWARD J JR"/AU) OR "BILLINGHAM K S"/AU OR ("BILLINGHAM M C J"/AU OR "BILLINGHAM M E"/AU OR "BILLINGHAM M E J"/AU OR "BILLINGHAM M J"/AU) OR ("BILLINGHAM MICHAEL"/AU OR "BILLINGHAM MICHAEL E"/AU OR "BILLINGHAM MICHAEL E J"/AU OR

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                "BILLINGHAM MICHAEL EDWARD JOHN"/AU OR "BILLINGHAM MICHAEL
                JOHN"/AU)
L36             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 AND L25
L37             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 NOT (L29 OR L34)


=>
=>

=> d ibib abs hitstr l37 1
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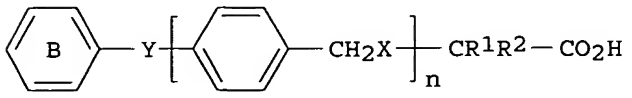
L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:783926 HCAPLUS
DOCUMENT NUMBER: 132:9040
TITLE: Aryl carboxylic acids which interact with the thyroid hormone receptor for the treatment of fibrotic disease
INVENTOR(S): **Billingham, Michael Edward John**; Fernihough, Janet Katherine
PATENT ASSIGNEE(S): Arthromics P.L.C., UK
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962507	A1	19991209	WO 1999-GB1684	19990527
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941547	A1	19991220	AU 1999-41547	19990527
EP 1083891	A1	20010321	EP 1999-925157	19990527
EP 1083891	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002516855	T2	20020611	JP 2000-551763	19990527
AT 234084	E	20030315	AT 1999-925157	19990527
ES 2194466	T3	20031116	ES 1999-925157	19990527
US 6348497	B1	20020219	US 2000-674512	20001116
US 2002049254	A1	20020425	US 2001-986820	20011113
US 6414026	B2	20020702		
US 2003018077	A1	20030123	US 2002-146919	20020517
US 2004180963	A1	20040916	US 2004-810682	20040329

PRIORITY APPLN. INFO.:

GB 1998-11784	A	19980602
GB 1998-27834	A	19981217
WO 1999-GB1684	W	19990527
US 2000-674512	A1	20001116
US 2001-986820	A1	20011113
US 2002-146919	A1	20020517

OTHER SOURCE(S): MARPAT 132:9040
GI



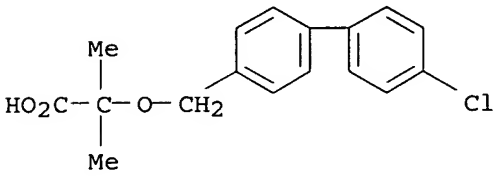
I

AB A method is provided for alleviating fibrotic disease by regulating tissue destructive proteolytic enzyme production in the presence of thyroid receptor binding but in the substantial absence of substantive corticosteroid and androgen receptor binding by administration of an effective amount of

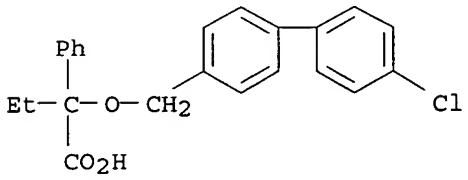
≥1 I [X = O, S, NH,SO2; Y = direct linkage, O, S, SO2, CR1R2 (R1, R2 = H, alkyl, aryl); ring B may be optionally substituted by ≥1 halo, alkyl, aryl radicals; n = 0, 1], and esters, amides, and salts thereof. Also provided is the use of ≥1 I in the preparation of a medicament in such a method.

IT **22494-47-9 80565-35-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl carboxylic acids interacting with thyroid hormone receptor for treatment of fibrotic disease)

RN 22494-47-9 HCAPLUS
CN Propanoic acid, 2-[(4'-chloro[1,1'-biphenyl]-4-yl)methoxy]-2-methyl- (9CI) (CA INDEX NAME)



RN 80565-35-1 HCAPLUS
CN Benzeneacetic acid, α-[(4'-chloro[1,1'-biphenyl]-4-yl)methoxy]-α-ethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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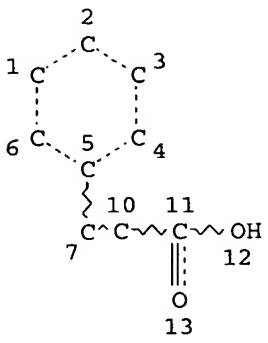


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NSPEC   IS RC     AT   7
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
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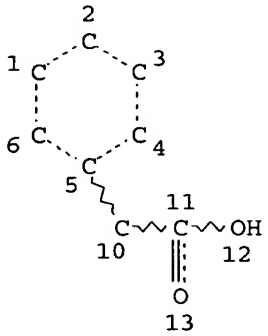


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   5
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
L4                STR
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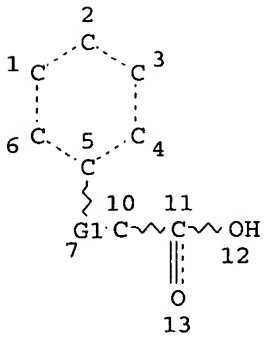
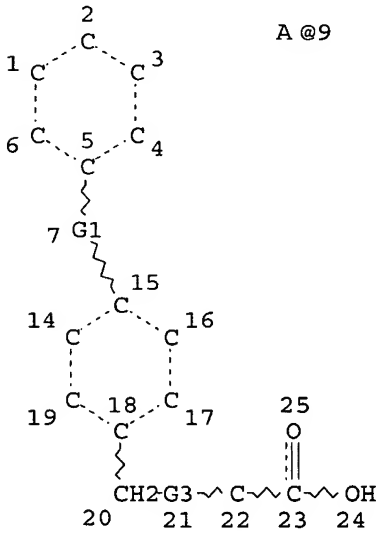


VAR G1=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 5
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L5 STR



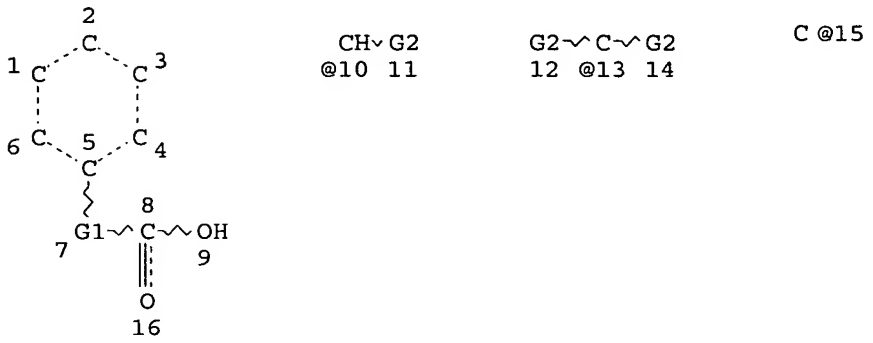
REP G1=(0-1) 9
VAR G3=O/S/N
NODE ATTRIBUTES:
NSPEC IS RC AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 14 5
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L6 105668 SEA FILE=REGISTRY SSS FUL L3 OR L4 OR L5

L14 204237 SEA FILE=HCAPLUS ABB=ON PLU=ON ("DIABETES MELLITUS"/CV OR DIABETES/CV) OR "ANTIDIABETIC AGENTS"/CV OR HYPERGLYCEMIA/CV OR ?DIABET? OR ?HYPERGLYCEM? OR (BLD OR BLOOD)(2A)(SUGAR OR GLUCOSE) OR MUSCULAR DYSTROPHY/CV OR DYSTROPHY/CV OR MYODYSTROPHY/CV OR ?DYSTROPHY? OR ?SCLEROS?(2A)SYSTEM?

L19 STR

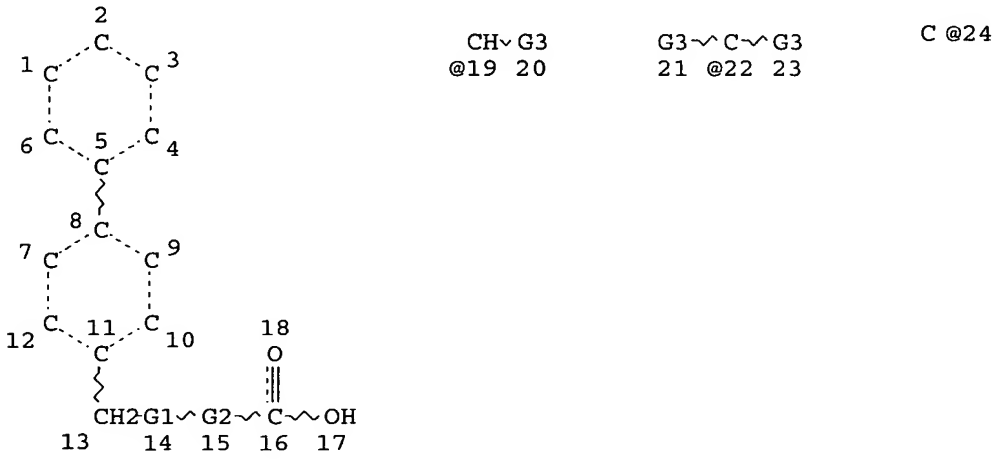


VAR G1=CH2/10/13/15
VAR G2=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L20 STR

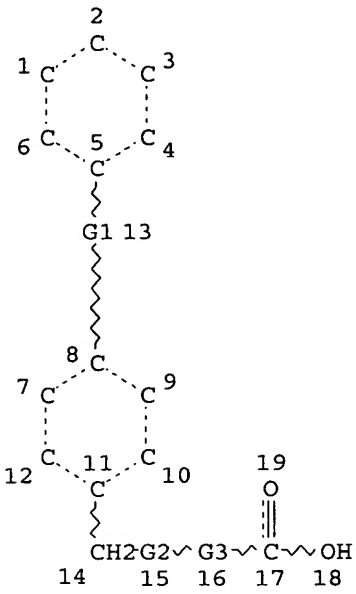


VAR G1=O/S/NH/SO2
VAR G2=CH2/19/22/24
VAR G3=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 24
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L21 STR



VAR G1=O/S/SO2/CH2/20/23/25
VAR G2=O/S/NH/SO2
VAR G3=CH2/20/23/25
VAR G4=CY/ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
NODE ATTRIBUTES:
NSPEC IS R AT 25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
L22 288559 SEA FILE=REGISTRY ABB=ON PLU=ON L2 OR L6
L24 27972 SEA FILE=REGISTRY SUB=L22 SSS FUL L19 OR L20 OR L21
L25 58477 SEA FILE=HCAPLUS ABB=ON PLU=ON L24
L26 283 SEA FILE=HCAPLUS ABB=ON PLU=ON L14(L)L25
L27 114 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 AND PD=<MAY 28, 1999
L28 7507 SEA FILE=HCAPLUS ABB=ON PLU=ON L25(L)(?MEDIC? OR ?THERAP? OR ?DRUG? OR ?PHARMA?)
L29 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L28
L30 1470 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L25
L31 389 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND PD=<MAY 28, 1999
L32 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND L31
L33 48 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 NOT L29
L34 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L33 AND PATENT/DT
L35 66 SEA FILE=HCAPLUS ABB=ON PLU=ON ("BILLINGHAM E J JR"/AU OR "BILLINGHAM EDWARD J JR"/AU) OR "BILLINGHAM K S"/AU OR ("BILLINGHAM M C J"/AU OR "BILLINGHAM M E"/AU OR "BILLINGHAM M E J"/AU OR "BILLINGHAM M J"/AU) OR ("BILLINGHAM MICHAEL"/AU OR "BILLINGHAM MICHAEL E"/AU OR "BILLINGHAM MICHAEL E J"/AU OR

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                "BILLINGHAM MICHAEL EDWARD JOHN"/AU OR "BILLINGHAM MICHAEL
                JOHN"/AU)
L36           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 AND L25
L37           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 NOT (L29 OR L34)
L38          79 SEA FILE=REGISTRY ABB=ON  PLU=ON  THYROID HORMONE RECEPTOR?/CN

L39        4439 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR (THYROID(W)HORMONE)(2A)
                RECEPTOR?
L40        4202 SEA FILE=HCAPLUS ABB=ON  PLU=ON  FIBROT?
L41           0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L35 AND (L39 OR L40)) NOT
                (L29 OR L34 OR L37)
L42          65 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L35 OR L41) NOT L37


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=> d ibib abs l42 1-6
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L42 ANSWER 1 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:819558 HCAPLUS
TITLE: Method of producing a pattern
INVENTOR(S): **Billingham, Michael John**
PATENT ASSIGNEE(S): Michael J. Billingham Limited, UK
SOURCE: Brit. UK Pat. Appl., No pp. given
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2279026	A1	19941221	GB 1993-12450	19930616
PRIORITY APPLN. INFO.:			GB 1993-12450	19930616

AB Unavailable

L42 ANSWER 2 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:234350 HCAPLUS
DOCUMENT NUMBER: 143:244468
TITLE: Development of an assay for the quantification of type I collagen synthesis in the guinea pig
AUTHOR(S): Quasnichka, Helen L.; Tarlton, John F.; Anderson-MacKenzie, Janet M.; **Billingham, Michael E. J.**; Bailey, Allen J.; Pickford, Andrew R.
CORPORATE SOURCE: Matrix Biology Research Group, University of Bristol, Bristol, Langford, BS40 7DY, UK
SOURCE: Journal of Immunological Methods (2005), 297(1-2), 133-141
CODEN: JIMMBG; ISSN: 0022-1759
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is a need for a reliable assay for the quantification of collagen type I synthesis in the guinea pig, an important model for many connective tissue diseases. Procollagen type I C-terminal propeptide (PICP) is the established marker of type I collagen synthesis but, to date, no assay was developed to measure PICP in guinea pig tissue exts. A monoclonal antibody, known to cross-react with intact guinea pig procollagen type I (anti-PICP), was tested for its ability to bind soluble guinea pig PICP in crude skin exts. using a biosensor. Anti-PICP was immobilized to the surface of a sensor chip and antibody-antigen binding was detected using the phenomenon of surface plasmon resonance (SPR). The binding component in the SPR-immunoassay was identified as PICP by purification and N-terminal sequencing. Guinea pig PICP was purified from skin by gel filtration, ion exchange chromatog. and lectin affinity chromatog. Purified PICP was then biotinylated and used with anti-PICP to develop a competition ELISA that was able to selectively and sensitively measure PICP in exts. of guinea pig connective tissue.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 3 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:776329 HCAPLUS
TITLE: Fundamental subchondral bone changes in spontaneous knee osteoarthritis
AUTHOR(S): Anderson-MacKenzie, Janet M.; Quasnichka, Helen L.; Starr, Roger L.; Lewis, E. Jonathan; **Billingham, Michael E. J.**; Bailey, Allen J.
CORPORATE SOURCE: Collagen Research Group, University of Bristol, Bristol, BS40 7DY, UK
SOURCE: International Journal of Biochemistry & Cell Biology (2004), Volume Date 2005, 37(1), 224-236
CODEN: IJBBFU; ISSN: 1357-2725
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Osteoarthritis has an unknown etiol., and tissue samples from early stage human osteoarthritis tissue cannot be reliably obtained. Therefore understanding the development of OA relies on using animal models: such as the spontaneous changes seen in the Dunkin-Hartley guinea pig strain, which are biochem., histol. and radiol. similar to human OA. We investigated the role of bone change in early OA development using the non-OA developing Bristol strain-2 as control from 3 to 36 wk by standard microfocal X-ray imaging and histol. techniques. The patella, tibia and femur epiphyseal region and immediate subchondral area were analyzed for bone d. at all ages. We found that both radiol. and histol. osteoarthritis scores increased progressively for the Dunkin-Hartley, but not for the BS2 demonstrating its value as a control. The Dunkin-Hartley had a higher bone d. and greater subchondral bone thickness from 24 wk of age. We conclude that prior to any gross osteoarthritis pathol. the Dunkin-Hartley are undergoing subchondral bone remodelling, thus demonstrating the fundamental role of early bone remodelling in the development of osteoarthritis.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 4 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:714385 HCAPLUS
DOCUMENT NUMBER: 142:128210
TITLE: Extended haplotypes and linkage disequilibrium in the IL1R1-IL1A-IL1B-IL1RN gene cluster: association with knee osteoarthritis
AUTHOR(S): Smith, A. J. P.; Keen, L. J.; **Billingham, M. J.**; Perry, M. J.; Elson, C. J.; Kirwan, J. R.; Sims, J. E.; Doherty, M.; Spector, T. D.; Bidwell, J. L.
CORPORATE SOURCE: Homoeopathic Hospital Site, University of Bristol Department of Pathology and Microbiology, Bristol, UK
SOURCE: Genes and Immunity (2004), 5(6), 451-460
CODEN: GEIMA2; ISSN: 1466-4879
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interleukin-1 gene cluster is a key regulator in a number of chronic disease processes. We explored the linkage between nine polymorphic loci in the IL1R1 promoter, eight in the IL1A-IL1B-IL1RN gene complex, and their association with osteoarthritis (OA), a common complex disease associated with low-level inflammation. Using 195 healthy controls, we identified eight novel polymorphisms in the IL1R1 exon 1A region. We found limited LD between IL1R1 and the IL1A-IL1B-IL1RN cluster, although LD within these two individual groups was high. To test association with knee OA, we genotyped 141 patients from Bristol (UK) at the 17 loci. IL1R1 promoter haplotypes showed no association with disease. However, within the IL1A-IL1B-IL1RN complex, we identified a common haplotype conferring a four-fold risk of OA (P=0.00043; Pc=0.0043) and one IL1B-IL1RN haplotype conferring a four-fold reduced risk (P=0.0036; Pc=0.029). To replicate these assocns., we subsequently examined 163 knee OA patients from London. Here, the effects of the haplotypes were confirmed: the risk IL1A-IL1B-IL1RN haplotype conferred a two-fold risk of OA (P=0.02), and the protective IL1B-IL1RN haplotype conferred a five-fold reduced risk of OA (P=0.0000008). These results may help to explain the genome-wide scan linkage data and functional observations concerning association between IL-1 and OA.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:373990 HCAPLUS
DOCUMENT NUMBER: 135:298446
TITLE: New mechanisms of action of mycophenolate mofetil in transplant recipients by assessment of its pharmacodynamics
AUTHOR(S): Barten, M. J.; van Gelder, T.; Gummert, J. F.; Shorthouse, R.; Boeke, K.; **Billingham, M. E.** ; Morris, R. E.
CORPORATE SOURCE: Department of Cardiothoracic Surgery, Transplantation Immunology, Stanford University Medical School, Stanford, CA, USA
SOURCE: Transplantation Proceedings (2001), 33(3), 2254-2255
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanism of action of mycophenolate mofetil (MMF) was studied by observing the pharmacodynamics (PD) of MMF in treated rat heart transplant recipients by expanding on previous PD methods in MPA-treated normal rats. All allograft groups were comprised of six rats each and were treated once daily with 5, 10, or 20 mg/kg of MMF by oral gavage beginning on the day of transplantation. MMF suppressed many lymphocyte functions in addition to its antiproliferative effects and that PD suppression of graft rejection was reflected by the immunosuppressive effects on peripheral blood lymphocytes in the model. PD studies offered the opportunity to define effects and mechanisms of action of immunosuppressive drugs in vivo and PD could be a useful means of monitoring MMF therapy to optimize treatment.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 6 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:373942 HCAPLUS
DOCUMENT NUMBER: 135:282888
TITLE: Mycophenolate mofetil pharmacodynamics and pharmacokinetics correlate with rejection score in a BN-to LEW heterotopic heart transplant model
AUTHOR(S): Klupp, J.; van Gelder, T.; Dambrin, C.; Regieli, J.; Boeke, K.; **Billingham, M. E.**; Morris, R. E.
CORPORATE SOURCE: Transplantation Immunology, Department of Cardiothoracic Surgery, Stanford Medical School, Stanford, CA, USA
SOURCE: Transplantation Proceedings (2001), 33(3), 2170-2171
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The correlation of mycophenolate mofetil (MMF) pharmacodynamics with the rejection score in a standard heart transplant model was evaluated by whole blood assay and compared the efficacy of MMF QD with BID treatments. Adult male Lewis and Brown Norway rats were used for intraabdominal heterotopic heart transplantation (BN to LEW). The animals were treated daily with 5 mg/kg MMF BID or 10 mg/kg MMF QD oral gavage until day 6, when pharmacokinetic/pharmacodynamic (P/D) study was performed. MPA and MPAG plasma levels were measured using high performance liquid chromatog. Whole blood was mitogen stimulated (ConA) for 72 h and proliferation (PCNA/DNA content) and expression of a variety of lymphocyte activation markers (CD25, CD71, CD11a, CD54) were measured using flow cytometry and normalized to pretreatment values. Heterotopic heart allografts showed significantly less rejection under MMF 5 mg/kg BID (5BID) treatment than under 10 mg/kg QD treatment. The proliferation assay (r2 = 0.81) showed the highest correlation with the scores for histol. severity of rejection. Higher MMF doses of 10 mg/kg BID and 20 mg/kg QD reached Emax in the pharmacodynamic assays, resulting in the rejection scores that were not significantly different from the 5 mg/kg BID group. In an novel PD assay, a high correlation among certain measures of immune function PD, PK, and rejection scores was shown. PD correlates higher with graft outcome than PK. Pharmacodynamic parameters showed immunosuppressive effects throughout the dosing period in the BID but not in the QD treatment group.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L42 ANSWER 6 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:373942 HCAPLUS
DOCUMENT NUMBER: 135:282888
TITLE: Mycophenolate mofetil pharmacodynamics and pharmacokinetics correlate with rejection score in a BN-to LEW heterotopic heart transplant model
AUTHOR(S): Klupp, J.; van Gelder, T.; Dambrin, C.; Regieli, J.; Boeke, K.; **Billingham, M. E.**; Morris, R. E.
CORPORATE SOURCE: Transplantation Immunology, Department of Cardiothoracic Surgery, Stanford Medical School, Stanford, CA, USA
SOURCE: Transplantation Proceedings (2001), 33(3), 2170-2171
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 7 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:491483 HCAPLUS
DOCUMENT NUMBER: 133:348674
TITLE: Differential expression pattern of membrane-type matrix metalloproteinases in rheumatoid arthritis
AUTHOR(S): Pap, Thomas; Shigeyama, Yukio; Kuchen, Stefan; Fernihough, Janet K.; Simmen, Beat; Gay, Renate E.; **Billingham, Michael**; Gay, Steffen
CORPORATE SOURCE: WHO Collaborating Center for Molecular Biology and Novel Therapeutic Strategies for Rheumatic Diseases, University Hospital, Zurich, Switz.
SOURCE: Arthritis & Rheumatism (2000), 43(6), 1226-1232
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: to study the expression of mRNA for different membrane-type matrix metalloproteinases (MT-MMPs) and compare their expression pattern in rheumatoid arthritis (RA) and normal synovium. Methods: Polymerase chain reaction (PCR) with specific primers was performed to analyze the presence of MT1-, MT2-, MT3-, and MT4-MMP in synovial tissue and synovial fibroblasts from 10 patients with RA and 4 subjects without arthritis. In addition, in situ hybridization with digoxigenin-labeled RNA probes was used to investigate the expression pattern of MT-MMPs in the synovium of these subjects. MT-MMP-expressing cells were characterized by immunohistochem. double labeling with anti-CD68 monoclonal antibodies. Results: Reverse transcription-PCR revealed the expression of MT1-, MT2-, MT3-, and MT4-MMP mRNA in all tissues and cell cultures examined However, in situ hybridization showed considerable differences in the expression pattern of the different MT-MMPs in RA synovium. MT1- and MT3-MMP mRNA were highly expressed in both the lining and the sublining layer, with more intense staining in the lining. Immunohistochem. double labeling demonstrated the presence of mRNA for MT1-MMP in fibroblasts and macrophages, as well as in osteoclast-like cells at sites of bone resorption. Expression of MT3-MMP mRNA was seen in fibroblasts and some macrophages. Expression of MT2- and MT4-MMP was characterized by staining of only a few CD68-neg. fibroblasts, and no differences could be found between the lining and sublining. Normal synovial samples showed only limited staining for all MT-MMPs. Conclusion: the authors' results indicate a role for MT1-MMP not only in the matrix degradation by fibroblasts, but also in osteoclast-mediated bone resorption in RA. Given the ability of MT1-MMP to activate MMP-2 and MMP-13, the findings also point to a cooperation between fibroblasts and macrophages in degrading cartilage and bone. While MT3-MMP is also intensely expressed in RA synovium, MT2- and MT4-MMP appear not to be involved in rheumatoid joint destruction.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 8 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:439934 HCAPLUS
DOCUMENT NUMBER: 133:162639
TITLE: Alterations in insulin-like growth factor binding protein-3 proteolysis and complex formation in the arthritic joint
AUTHOR(S): Whellams, E. J.; Maile, L. A.; Fernihough, J. K.; **Billingham, M. E. J.**; Holly, J. M. P.
CORPORATE SOURCE: Department of Surgery, Division of Hospital Medicine, University of Bristol, Bristol Royal Infirmary, Bristol, BS2 8HW, UK
SOURCE: Journal of Endocrinology (2000), 165(3), 545-556
CODEN: JOENAK; ISSN: 0022-0795
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Increased concns. of insulin-like growth factor (IGF) system components have previously been observed in rheumatoid arthritis (RA) and osteoarthritis (OA); however, disruption of the IGF axis and the implications for the disease process remain largely unaddressed. This study was undertaken to characterize the IGF binding protein (IGFBP)-3 proteolysis and complex formation systems in synovial fluid and to investigate changes in these systems in arthritic disease, and their impact on the availability of IGF. Western blotting or autoradiog. of SDS gels was used to visualize IGFBP-3 or its proteolysis. IGF-I and IGFBP-3 concns. were determined by RIAs and acid-labile subunit (ALS) was measured by ELISA. A shift in distribution of IGFBP-3 and IGF-I in RA and OA synovial fluids (RASynF, OASynF) and an associated increase in ALS suggested the presence of 150 kDa ternary complexes. IGFBP-3 proteolysis was decreased in RASynF and OASynF, but was apparent in size-fractionated fluid and resembled serum activity. The presence of serum-like inhibitors of IGFBP-3 proteolysis in RASynF was also demonstrated by the ability of this fluid, and 150 kDa fractions from its size fractionation, to inhibit IGFBP-3 proteolysis in the other synovial fluid. A marked disruption in the IGF system was observed, as considerably more IGF-I was retained in ternary complexes. The authors also classified the IGFBP-3 proteolysis system in synovial fluid and found it to be disturbed in RASynF and OASynF. These changes may be caused by an increased flux of circulatory proteins into synovial fluid, resulting from an inflammation-induced increase in vascular permeability. The net result in RA and OA would be a decrease in IGF availability in arthritic joints, and therefore loss of a potential anabolic stimulus. This disruption to the IGF axis would influence disease progression in RA and OA.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 9 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:300056 HCAPLUS
DOCUMENT NUMBER: 131:128624
TITLE: Collagen Remodeling in the Anterior Cruciate Ligament Associated with Developing Spontaneous Murine Osteoarthritis
AUTHOR(S): Anderson-MacKenzie, Janet M.; **Billingham, Michael E.**; Bailey, Allen J.
CORPORATE SOURCE: Collagen Research Group, Division of Molecular and Cellular Biology, University of Bristol, Langford Bristol, BS40 5DS, UK
SOURCE: Biochemical and Biophysical Research Communications (1999), 258(3), 763-767
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The initiating factors in primary, idiopathic osteoarthritis are unknown, the characteristic bone and cartilage changes being late features of the disease. We have proposed that biochem. cruciate ligament alteration may be important in early osteoarthritis by mediating loading consequences on the bone and cartilage. Using the widely accepted STR/ORT mouse model of spontaneous osteoarthritis we have found biochem. evidence that, before radiol. signs of osteoarthritis develop, cruciate ligament collagen metabolism is upregulated in the STR/ORT mouse when compared to controls. Also, importantly, at this time the anterior cruciate ligament is weaker in STR/ORT mice than in controls. This is the first biochem. evidence to show that alterations in cruciate ligament metabolism occur early in the etiopathogenesis of idiopathic, primary osteoarthritis. (c) 1999 Academic Press.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 10 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:439935 HCAPLUS
DOCUMENT NUMBER: 125:113708
TITLE: Phosphorus availability from phosphate rock as enhanced by water-soluble phosphorus
AUTHOR(S): Chien, S. H.; Menon, R. G.; **Billingham, K. S.**
CORPORATE SOURCE: Research and Development Division, International fertilizer Development Center, Muscle Shoals, AL, 35662, USA
SOURCE: Soil Science Society of America Journal (1996), 60(4), 1173-1177
CODEN: SSSJD4; ISSN: 0361-5995
PUBLISHER: Soil Science Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radioactive 32P was used as a tracer to distinguish P availability from soil, phosphate rock (PR), triple superphosphate (TSP) so that P uptake by crops from PR in the presence of TSP could be estimated Three sets of 4-kg soil samples of an acid Hartsells silt loam (fine-loamy, siliceous, thermic Typic Hapludult, pH 4.8) were mixed with the following treatments: (i) 32P solution and central Florida PR (CFPR), (ii) 32P-tagged TSP, and (iii)32P-tagged TSP and CFPR at a P ratio of 50:50. The rates of P applied were 0, 12.5, 25, 50, 100, and 200 mg P kg-1. For treatment (iii), an addnl. rate of 400 mg P kg-1 was also prepared Maize (Zea mays L.) and cowpea (Vigna unguiculata unguiculata) were planted and harvested at 42 d after planting for maize and 45 d for cowpea. The effectiveness of P sources in terms of increasing dry-matter yield and P untake followed the order of TSP > (CFPR + TSP) > CFPR for maize and TSP = (CFPR + TSP) > CFPR for cowpea. Phosphorus uptake from CFPR in the presence of TSP was higher than P uptake from CFPR applied alone, indicating an enhancement effect of TSP on the effectiveness of CFPR. The increase in P uptake from CFPR due to TSP influence, across all the PR rates applied, was 3.48 mg P pot-1 for maize and 1.38 mg P pot-1 for cowpea. With respect to P uptake from CFPR applied alone, the corresponding relative increase in P uptake from CFPR due to TSP influence was 165% for maize and 72% for cowpea.

L42 ANSWER 11 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:139708 HCAPLUS
DOCUMENT NUMBER: 124:229285
TITLE: A 71-kD heat shock protein (hsp) from Mycobacterium tuberculosis has modulatory effects on experimental rat arthritis
AUTHOR(S): Kingston, A. E.; Hicks, C. A.; Colston, M. J.; **Billingham, M. E. J.**
CORPORATE SOURCE: Lilly Research Centre Ltd., Eli Lilly and Company, Windlesham, GU206PH, UK
SOURCE: Clinical and Experimental Immunology (1996), 103(1), 77-82
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of a mycobacterial 71 kDa hsp antigen have been investigated for its ability to modulate arthritis in rats. S.c. injection (base of tail) of increasing amts. of hsp71 from Mycobacterium tuberculosis (MTB) produced dose-dependent differential inhibitory effects on induction of arthritis by MTB and CP20961 in rats. As little as 1 μg of the hsp71 produced a reduction in MTB arthritis, whereas complete protection was observed when 50 μg were administered. When 71-kD-treated rats were challenged with CP20961, all developed reduced symptoms of arthritis compared with control rats, but in this model no complete protection was observed over the dose range studied. The effects of 71 kDa pretreatment on collagen II arthritis were not significant, but in general symptoms of arthritis were milder than in the control group. The same pattern of results was observed previously when hsp65 was used in the different models. These results show that the modulatory effects of hsp on adjuvant arthritis are not restricted to the hsp65 series, but are also mediated by a member of the hsp70 family.

L42 ANSWER 12 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:1002132 HCAPLUS
DOCUMENT NUMBER: 124:175758
TITLE: The anti-rheumatic potential of a series of 2,4-di-substituted-4H-naphtho[1,2-b]pyran-3-carbonitriles
AUTHOR(S): Smith, Colin W.; Bailey, James M.; **Billingham, Michael E. J.**; Chandrasekhar, Srinivasan; Dell, Colin P.; Harvey, Anita K.; Hicks, Caroline A.; Kingston, Ann E.; Wishart, Graham N.
CORPORATE SOURCE: Lilly Res. Centre Ltd., Eli Lilly & Co., Surrey, GU20 6PH, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(23), 2783-8
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new series of naphtho[1,2-b]pyran-3-carbonitriles with enhanced stability under acid conditions has been synthesized and examined for antiproliferative and anti-inflammatory activity. 4-(3-Nitrophenyl)-2-(N-succinimido)-4H-naphtho[1,2-b]pyran-3-carbonitrile has proved to be acid stable and still retains biol. activity.

L42 ANSWER 13 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:816545 HCAPLUS
DOCUMENT NUMBER: 123:336129
TITLE: Adjuvant arthritis: The first model
AUTHOR(S): **Billingham, M. E. J.**
CORPORATE SOURCE: Medical School, University Utah, Salt Lake City, UT, 84132, USA
SOURCE: Mechanisms and Models in Rheumatoid Arthritis (1995), 389-409. Editor(s): Henderson, Brian; Edwards, Jonathan C. W.; Pettipher, E. R. Academic: London, UK.
CODEN: 61SFAI
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 78 refs.

L42 ANSWER 14 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:709778 HCAPLUS
DOCUMENT NUMBER: 123:102312
TITLE: Studies in experimental models of chronic rejection: Use of rapamycin (sirolimus) and isoxazole derivatives (leflunomide and its analog) for the suppression of graft vascular disease and obliterative bronchiolitis
AUTHOR(S): Morris, R. E.; Huang, X.; Gregory, C. R.; **Billingham, M. E.**; Rowan, R.; Shorthouse, R.; Berry, G. J.
CORPORATE SOURCE: School Medicine, Stanford University, Stanford, CA, USA
SOURCE: Transplantation Proceedings (1995), 27(3), 2068-9
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Appleton & Lange
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rapamycin and leflunomide suppression of graft vascular disease and obliterative bronchiolitis was studied.

L42 ANSWER 15 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:583225 HCAPLUS
DOCUMENT NUMBER: 123:30683
TITLE: Increased proteoglycan synthesis in cartilage in experimental canine osteoarthritis does not reflect a permanent change in chondrocyte phenotype
AUTHOR(S): Venn, G.; **Billingham, M. E. J.**; Hardingham, T. E.
CORPORATE SOURCE: Kennedy Institute Rheumatology, London, W6 7DW, UK
SOURCE: Arthritis & Rheumatism (1995), 38(4), 525-32
CODEN: ARHEAW; ISSN: 0004-3591
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To determine whether chondrocytes in early exptl. osteoarthritic (OA) cartilage continue to show increased synthesis and turnover of proteoglycans (PGs) during explant culture. A comparison was also made between the responsiveness of exptl. OA and control cartilage to interleukin-1β (IL-1β) and tumor necrosis factor α (TNFα) after 1 day and 3 days in culture. OA was induced in mature animals by sectioning of the anterior cruciate ligament followed by 3 mo of normal exercise. PG synthesis in the articular cartilage was determined by measuring 35S-sulfate incorporation during explant culture over 1-3 days. Inhibition of PG synthesis was also determined with various concns. of IL-1β and TNFα after 1 and 3 days in culture. PGs extracted from the articular cartilage over 1-3 days in culture were examined by agarose PAGE. Up to 24 h after excision from the joint, PG synthesis was higher in exptl. OA cartilage than in control cartilage. It was also less sensitive to inhibition by TNFα. These differences were no longer detected after 48-72 h in culture. There were no changes in the relative proportions of aggrecan and decorin/biglycan extracted from and synthesized by control and exptl. OA cartilage over the 3 days in culture. Previous results indicated that PG synthesis and turnover in articular cartilage was increased for many months after induction of exptl. OA. The present results show that the enhanced rate of PG synthesis and turnover were evident in freshly explanted tissue, but the differences were lost over 3 days in culture. A decreased responsiveness to TNFα was also lost. The hypermetabolic activity of exptl. OA chondrocytes was thus reversible and not a permanent change in chondrocyte phenotype.

L42 ANSWER 16 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:551648 HCAPLUS
DOCUMENT NUMBER: 123:473
TITLE: Rapamycin (sirolimus) inhibits vascular smooth muscle DNA synthesis in vitro and suppresses narrowing in arterial allografts and in balloon-injured carotid arteries: Evidence that rapamycin antagonizes growth factor action on immune and nonimmune cells
AUTHOR(S): Morris, R. E.; Cao, W.; Huang, X.; Gregory, C. R.; **Billingham, M. E.**; Rowan, R.; Shorthouse, R. A.
CORPORATE SOURCE: Departments Cardiothoracic Surgery and Pathology, Stanford University School Medicine, Stanford, CA, 94305-5247, USA
SOURCE: Transplantation Proceedings (1995), 27(1), 430-1
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rapamycin inhibits growth factor-stimulated vascular smooth muscle cell DNA synthesis in vitro. This effect of rapamycin may be mediated through complexes of rapamycin with FKBP. The results indicate that rapamycin may have potential therapeutic benefit in controlling vascular manifestations of chronic rejection as well as arterial narrowing after balloon angioplasty.

L42 ANSWER 17 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:602679 HCAPLUS
DOCUMENT NUMBER: 121:202679
TITLE: Monoclonal antibody therapy of experimental arthritis: comparison with cyclosporin A for elucidating cellular and molecular disease mechanisms
AUTHOR(S): **Billingham, M. E. J.**
CORPORATE SOURCE: Lilly Res. Cent. Ltd., Windlesham/Surrey, GU20 6PH, UK
SOURCE: Immunopharmacol. Jt. Connect. Tissue (1994), 65-86.
Editor(s): Davies, M. Elisabeth; Dingle, John T.
Academic: London, UK.
CODEN: 60QAAM
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 80 refs. on the therapeutic uses of monoclonal antibodies specific for the TCR receptor, the interleukin-2 receptor, and Ia antigens; polyarthritis models in the rat; tolerance induction with monoclonal antibodies; and remission mechanisms of rat polyarthritis.

L42 ANSWER 18 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:555543 HCAPLUS
DOCUMENT NUMBER: 121:155543
TITLE: Cross-reactivity to proteoglycans in bacterial arthritis: lack of evidence for in vivo role in induction of disease
AUTHOR(S): van de Langerijt, A. G. M.; Kingston, A. E.; van Lent, P. L. E. M.; **Billingham, M. E. J.**; van den Berg, W. B.
CORPORATE SOURCE: Dep. Rheumatol., Univ. Hosp. Nijmegen, Nijmegen, 6500 HB, Neth.
SOURCE: Clinical Immunology and Immunopathology (1994), 71(3), 273-80
CODEN: CLIIAT; ISSN: 0090-1229
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cross-reactivity between bacterial epitopes and cartilage components has been assumed to play a role in the pathol. of bacterial-induced arthritis models. In this study, the authors report prominent proteoglycan (PG) depletion in Safranin-O stained ankle joint sections from collagen-induced arthritic rats. In adjuvant arthritis and streptococcal cell wall-induced arthritis (SCW-A), however, only limited PG degradation was observed In vitro, PG fractions were able to stimulate T lymphocytes from these arthritic rats. To investigate the contribution of cross-reactivity, Lewis rats were primed with SCW in Freund's incomplete adjuvant (SCW/FIA). This immunization protocol resulted in in vitro stimulatory responses to the SCW antigens and cartilage PG antigens, but not to joint inflammation per se. Next, papain was injected intraarticularly to create a situation in which a large amount of potential cross-reactive cartilage epitopes are released. Interestingly, no inflammatory reaction could be observed in the papain-injected joints of SCW/FIA-primed rats. These data suggest that cross-reactivity between bacterial epitopes and PG does not seem to be a key element in the onset of joint inflammation in bacterial-induced arthritis. However, it cannot be ruled out that at later time points cross-reactivity will contribute to joint inflammation.

L42 ANSWER 19 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:6184 HCAPLUS
DOCUMENT NUMBER: 120:6184
TITLE: Cysteine proteinase activity in the development of arthritis in an adjuvant model of the rat
AUTHOR(S): Meijers, M. H. M.; Koopdonk-Kool, J.; Meacock, S. C. R.; Van Noorden, C. J. F.; Bunning, R. A. D.; **Billingham, M. E. J.**
CORPORATE SOURCE: Osteoarthritis Res., Lilly Res. Cent. Ltd., Windlesham, UK
SOURCE: Agents and Actions (1993), 39(Spec. Conf. Issue), C219-C221
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsin B and L activity was studied histochem. in arthritic rat ankle joints using specific synthetic substrates in a post coupling method on unfixed and undecalcified cryostat sections of rat ankle joints. Activity was strongly increased in chondrocytes and cells of the inflamed synovium with the development of arthritis induced by the synthetic adjuvant CP20961. Activity reached a maximum 20 days after induction of arthritis, and decreased as the rats entered natural remission. Cathepsin B and L were at their highest level when macrophages were present in the joint space, as shown by using monoclonal antibody markers for rat macrophages (ED1 and ED2) in a biotin-avidin immunoperoxidase assay. The results suggest that the macrophage infiltrate may have stimulated proteinase production in chondrocytes through cytokine release. The profile of appearance of cysteine proteinases suggests their involvement in the breakdown of cartilage and bone in the arthritic joint.

L42 ANSWER 20 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:601603 HCAPLUS
DOCUMENT NUMBER: 119:201603
TITLE: Elevated synovial fluid levels of interleukin-6 and tumor necrosis factor associated with early experimental canine osteoarthritis
AUTHOR(S): Venn, G.; Nietfeld, J. J.; Duits, A. J.; Brennan, F. M.; Arner, E.; Covington, M.; **Billingham, M. E. J.**; Hardingham, T. E.
CORPORATE SOURCE: Biochem. Div., Kennedy Inst. Rheumatol., London, W6 7DW, UK
SOURCE: Arthritis & Rheumatism (1993), 36(6), 819-26
CODEN: ARHEAW; ISSN: 0004-3591
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteoarthritis (OA) was induced in 12 mature animals by sectioning the anterior cruciate ligament. After 3 mo, synovial fluid (SF) from the operated and contralateral (control) knee joints was assayed for interleukin-6 (IL-6), tumor necrosis factor (TNF), IL-1, latent metalloproteinase, and sulfated glycosaminoglycans (GAG). Proteoglycan synthesis in the corresponding articular cartilage was also measured. IL-6 levels in SF from the operated joint compared with the control joint were significantly elevated in 11 of 12 animals. TNF levels were also elevated in 10 of 11 SF samples from operated joints, but to a lesser extent than those of Il-6. IL-1 and IL-1 inhibitors were undetectable in either the operated or control joint SF. The GAG concentration was elevated in SF from exptl. OA joints. This elevation correlated with that of TNF, but not IL-6. There was no significant difference in the concentration of APMA-activatable metalloproteinase. The rate of proteoglycan synthesis was higher in the cartilage from the operated joint in 8 of 12 animals, and the mean rate of synthesis was significantly higher than in the control joint. There was a pos. correlation between this increase in cartilage proteoglycan synthesis (operated vs. control) and the increase in SF IL-6, but there was no correlation with the levels of TNF or GAG. This is the first study of SF levels of cytokines in early exptl. OA. The authors' results show surprisingly high levels of IL-6 in operated joints, where the cytokine could act directly on the chondrocytes, and thus play a role in mediating their responses to cartilage injury.

L42 ANSWER 21 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:446825 HCAPLUS
DOCUMENT NUMBER: 119:46825
TITLE: In vitro and in vivo effects of proteoglycan fractions in adjuvant treated rats
AUTHOR(S): Kingston, A. E.; Carney, S. L.; Hicks, C. A.; **Billingham, M. E. J.**
CORPORATE SOURCE: Lilly Res. Cent., Windlesham/Surrey, GU20 6PH, UK
SOURCE: Agents and Actions Supplements (1993), 39(Joint Destruction in Arthritis and Osteoarthritis), 75-9
CODEN: AASUDJ; ISSN: 0379-0363
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Differential stimulatory effects by proteoglycan fractions: chondroitin (CS)- and keratan-sulfate regions; link protein and binding region were observed in cultures of spleen and lymph node lymphocytes taken from normal and adjuvant treated Lewis rats. In vivo, none of the fractions induced symptoms of arthritis but pretreatment with the CS rich region produced an inhibition of Mycobacterium tuberculosis-induced arthritis.

L42 ANSWER 22 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:420180 HCAPLUS
DOCUMENT NUMBER: 119:20180
TITLE: Simvastatin decreases accelerated graft vessel disease (GVD) after heart transplantation in an animal model
AUTHOR(S): Meiser, B. M.; Wenke, K.; Thiery, J.; Wolf, S.; Devens, C.; Seidel, D.; Hammer, C.; **Billingham, M. E.**; Reichart, B.
CORPORATE SOURCE: Dep. Card. Surg., Univ. Munich, Munich, 8000/70, Germany
SOURCE: Transplantation Proceedings (1993), 25(2), 2077-9
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to investigate the role of cholesterol metabolism in the development of accelerated GVD after HT in an exptl. model. Since HMG-CoA reductase is the key enzyme in the cholesterol biosynthesis, we tested the effect of the HMG-CoA reductase inhibitor, simvastatin, a methylated derivative of lovastatin, on GVD. This study shows, for the first time, that treatment with the HMG-CoA reductase inhibitor simvastatin significantly decreases FK 506-induced GVD in an exptl. rat allograft model.

L42 ANSWER 23 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:183074 HCAPLUS
DOCUMENT NUMBER: 118:183074
TITLE: Treatment with rapamycin blocks arterial intimal thickening following mechanical and alloimmune injury
AUTHOR(S): Gregory, C. R.; Huie, P.; Shorthouse, R.; Wang, J.; Rowan, R.; **Billingham, M. E.**; Morris, R. E.
CORPORATE SOURCE: Sch. Med., Stanford Univ., Stanford, CA, USA
SOURCE: Transplantation Proceedings (1993), 25(1, Book 1), 120-1
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The carotid artery thickening was studied in rats after balloon catheter-induced mech. injury or immune injury from allotransplantation of femoral artery graft. Both injuries caused substantial intimal thickening which was inhibited by rapamycin (1.5-6 mg/kg i.p. daily for 39 days) in the case of mech. injury. In the case of immune injury, only the higher doses were effective.

L42 ANSWER 24 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:183013 HCAPLUS
DOCUMENT NUMBER: 118:183013
TITLE: Effects of treatment with cyclosporine, FK 506, rapamycin, mycophenolic acid, or deoxyspergualin on vascular muscle proliferation in vitro and in vivo
AUTHOR(S): Gregory, C. R.; Pratt, R. E.; Huie, P.; Shorthouse, R.; Dzau, V. J.; **Billingham, M. E.**; Morris, R. E.
CORPORATE SOURCE: Sch. Med., Stanford Univ., Stanford, CA, USA
SOURCE: Transplantation Proceedings (1993), 25(1, Book 1), 770-1
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rapamycin (RPM) and mycophenolic acid (MPA) have pharmacol. effects in addition to their suppression of allograft rejection. In vivo, RPM and MPA were the most effective agents for preventing intimal smooth muscle thickening following arterial injury.

L42 ANSWER 25 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:167413 HCAPLUS
DOCUMENT NUMBER: 118:167413
TITLE: Computer-assisted densitometric analysis for quantification of cell surface antigen expression in monkey cardiac allografts: correspondence to histopathologic grade of rejection
AUTHOR(S): Kitamura, Masaya; Lackides, G. A.; **Billingham, M. E.**; Clayberger, C.; Starnes, V. A.
CORPORATE SOURCE: Heart Inst. Japan, Tokyo Women's Med. Coll., Tokyo, 162, Japan
SOURCE: Transplantation Proceedings (1993), 25(1, Book 2), 924-7
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A computer-assisted densitometric anal. characterized and quantified the expression of immune cell surface antigens (CD2, CD8, CD4, CD11a, class I, class II, CD39, CD28, CD45R, CD25, CD58, and CD54) in biopsy specimens from cynomolgus monkey cardiac allografts with various degrees of acute rejection. Computer-assisted densitometric anal. of cell surface antigen expression can be a useful technique for investigation of cardiac allograft rejection.

L42 ANSWER 26 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:38708 HCAPLUS
DOCUMENT NUMBER: 118:38708
TITLE: Novel immunosuppressive butenamides
AUTHOR(S): Axton, Christopher A.; **Billingham, Michael E. J.**; Bishop, Paul M.; Gallagher, Peter T.; Hicks, Terence A.; Kitchen, E. Ann; Mullier, Graham W.; Owton, W. Martin; Parry, Mark G.; et al.
CORPORATE SOURCE: Lilly Res. Cent. Ltd., Windlesham/Surrey, GU20 6PH, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1992), (17), 2203-13
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 2-[4-(1,1-Dimethylethyl)phenyl]thiophene was carboxylated using butyllithium and carbon dioxide to give 5-[4-(1,1-dimethylethyl)phenyl]thiophene-2-carboxylic acid. Conversion of the acid using di-Ph phosphazidate and triethylamine gave 5-[4-(1,1-dimethylethyl)phenyl]thiophene-2-carbonyl azide, which was rearranged in toluene at 110° with loss of nitrogen to give the isocyanate; this in turn was treated with sodium 1-cyanoprop-1-ene 2-oxide in THF to give 2-cyano-N-{5-[4-(1,1-dimethylethyl)phenyl]thiophen-2-yl}-3-hydroxybut-2-enamide (I). Analogous chemical has been utilized to synthesize both heteroarylphenylbutenamides, e.g., II and III and phenylbutenamides, e.g., IV (R= Cl, Bu, Me2CH, Me3C, EtMe2C, PrMe2C), which display immunosuppressive activity towards proliferating Con A-stimulated T-lymphocytes.

L42 ANSWER 27 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:645267 HCAPLUS
DOCUMENT NUMBER: 117:245267
TITLE: Continuous infusion of angiopeptin significantly reduces accelerated graft vessel disease induced by FK 506 in a rat heart allograft model
AUTHOR(S): Meiser, B. M.; Wolf, S.; Devens, C.; Wenke, K.; Thiery, J.; Kreuzer, E.; Hammer, C.; **Billingham, M. E.**; Reichart, B.
CORPORATE SOURCE: Dep. Card. Surg., Ludwig Maximilians Univ., Munich, 8000/70, Germany
SOURCE: Transplantation Proceedings (1992), 24(5), 1671-2
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Angiopeptin (25 or 100 μg/kg) attenuated the expression of graft vessel disease induced by FR 506 (4 mg/kg) in a rat heart allograft model, but did not change the rejection rate from that after FK 506 monotherapy.

L42 ANSWER 28 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:509342 HCAPLUS
DOCUMENT NUMBER: 117:109342
TITLE: Increased release of matrix components from articular cartilage in experimental canine osteoarthritis
AUTHOR(S): Ratcliffe, Anthony; **Billingham, Michael E. J.** ; Saed-Nejad, Fatemeh; Muir, Helen; Hardingham, Timothy E.
CORPORATE SOURCE: Dep. Orthop. Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: Journal of Orthopaedic Research (1992), 10(3), 350-8
CODEN: JOREDR; ISSN: 0736-0266
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The release rates of specific components of the proteoglycan aggregates (G1 domain, the chondroitin sulfate and keratan sulfate-containing portion of the protein core, and link protein) of the articular cartilage of mature beagles were studied at early stages of canine exptl. osteoarthritis (OA), generated by transection of the anterior cruciate ligament. Anal. of cartilage explants and synovial fluids indicates that at early stages of exptl. OA, there is increased release of the proteoglycan aggregates of the articular cartilage. This involves a release from the tissue of the components of the proteoglycan that are specifically involved with aggregation together with the glycosaminoglycans of the proteoglycan. These components were detected at elevated levels in the media of explants of cartilage from the operated joint, and in the synovial fluids of the operated joints.

L42 ANSWER 29 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:405463 HCAPLUS
DOCUMENT NUMBER: 117:5463
TITLE: Changes in proteoglycan turnover in experimental canine osteoarthritic cartilage
AUTHOR(S): Carney, S. L.; **Billingham, M. E. J.**; Caterson, B.; Ratcliffe, A.; Bayliss, M. T.; Hardingham, T. E.; Muir, H.
CORPORATE SOURCE: Biochem. Div., Kennedy Inst. Rheumatol., London, W6 7DW, UK
SOURCE: Matrix (Stuttgart) (1992), 12(2), 137-47
CODEN: MTRXEH; ISSN: 0934-8832
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The metabolism of newly synthesized and total (resident) proteoglycans was examined in control and osteoarthritic cartilage explants obtained from an exptl. model of canine osteoarthritis. Non-labeled proteoglycans extracted from normal cartilage with 4M guanidine HCl showed two bands visualized by staining with toluidine blue. The electrophoretic mobilities of proteoglycans from osteoarthritic cartilage were unchanged but the relative abundance of the slower migrating band increased with time after surgery. There were qual. differences in the proteoglycan breakdown products released into the medium of explant cultures of osteoarthritic compared with control cartilage. This was apparent for both labeled and total unlabeled proteoglycans. There were similarities in the electrophoretic mobilities of the major labeled and nonlabeled proteoglycan breakdown products suggesting that total (resident) proteoglycans and newly formed proteoglycans were degraded by similar mechanisms. There were however some differences in the labeled and non-labeled proteoglycans, suggesting that the mechanisms of breakdown were not identical. Immunoblotting techniques showed differences in the distribution of various glycosaminoglycans in proteoglycan breakdown products from control compared with osteoarthritic cartilage explant cultures. Monoclonal antibodies 7-D-4 and 3-B-3 (which recognize unusual native chondroitin sulfate epitopes) showed greatly increased expression on proteoglycans from osteoarthritic cartilage compared with controls.

L42 ANSWER 30 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:505658 HCAPLUS
DOCUMENT NUMBER: 115:105658
TITLE: Effects of the new and highly active immunosuppressant, rapamycin, on lymphoid tissues and cells in vivo
AUTHOR(S): Zheng, B.; Shorthouse, R.; Masek, M. A.; Berry, G.; **Billingham, M. E.**; Morris, R. E.
CORPORATE SOURCE: Sch. Med., Stanford Univ., Stanford, CA, 94305-5247, USA
SOURCE: Transplantation Proceedings (1991), 23(1, Bk. 1), 851-5
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of rapamycin on the structure, cell populations, and cell functions of the central and peripheral lymphoid tissues in mice were studied and compared to FK 506. Results show that the effects of rapamycin and FK 506 are different.

L42 ANSWER 31 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:137193 HCAPLUS
DOCUMENT NUMBER: 112:137193
TITLE: A mycobacterial 65-kD heat shock protein induces antigen-specific suppression of adjuvant arthritis, but is not itself arthritogenic
AUTHOR(S): **Billingham, M. E.**; Carney, S.; Butler, R.; Colston, M. J.
CORPORATE SOURCE: Lilly Res. Cent. Ltd., Eli Lilly and Co., Windlesham/Surrey, GU20 6PH, UK
SOURCE: Journal of Experimental Medicine (1990), 171(1), 339-44
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A recombinant (r)65-kD protein from Mycobacterium leprae, at levels far in excess of those present in whole mycobacteria, was unable to induce arthritis. Even when combined with a synthetic adjuvant, CP20961, to mimic the peptidoglycan adjuvant component of the mycobacterial cell wall, the r65-kD protein failed to induce arthritis. Pretreatment with as little as 1 μg r65-kD protein protected rats against arthritis induced by M. tuberculosis, but this r65-kD protein was markedly less able to protect against arthritis induced by the synthetic adjuvant, CP20961, or type II collagen. The r65-kD protein appears, therefore, to produce an antigen-specific protection against arthritis induced by bacterial cell walls containing the 65-kD protein. Such protection can be overcome, however, by arthritogenic T lymphocytes, suggesting that protection occurs by preventing clonal proliferation of autoreactive T lymphocytes that are induced by the adjuvant properties of mycobacterial cell walls.

L42 ANSWER 32 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:629851 HCAPLUS
DOCUMENT NUMBER: 111:229851
TITLE: Acute phase proteins
AUTHOR(S): Whicher, J. T.; Thompson, D.; **Billingham, M. E. J.**; Kitchen, E. Ann
CORPORATE SOURCE: Old Med. Sch., Univ. Leeds, Leeds, LS2 9JT, UK
SOURCE: Modern Methods in Pharmacology (1989), 5(Pharmacol. Methods Control Inflammation), 101-28
CODEN: MMEPDE; ISSN: 0732-7218
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with .apprx.110 refs. of the classification of acute-phase proteins, acute-phase protein synthesis, interspecies and sex differences, and in vivo and in vitro models of inflammation for the study of acute-phase proteins.

L42 ANSWER 33 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:475651 HCAPLUS
DOCUMENT NUMBER: 107:75651
TITLE: Cytokines as inflammatory mediators
AUTHOR(S): **Billingham, M. E. J.**
CORPORATE SOURCE: Lilly Res. Cent. Ltd., Windlesham/Surrey, GU20 6PH, UK
SOURCE: British Medical Bulletin (1987), 43(2), 350-70
CODEN: BMBUAQ; ISSN: 0007-1420
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 64 refs. of biochem. properties, production, and cell targets and biol. effects of inflammatory cytokines (especially interleukin 1 and tumor necrosis factor). Control mechanisms for release and activity of cytokines in inflammation are also discussed.

L42 ANSWER 34 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:619621 HCAPLUS
DOCUMENT NUMBER: 105:219621
TITLE: Possible attenuation of graft atherosclerosis by prostaglandin E analogs
AUTHOR(S): Aziz, S.; **Billingham, M. E.**; Jamieson, S. W.
CORPORATE SOURCE: Med. Cent., Stanford Univ., Stanford, CA, 94305, USA
SOURCE: Transplantation Proceedings (1986), 18(5, Suppl. 4), 71-6
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Both cyclosporin A [59865-13-3] (1-2 mg/kg/day, i.m.) and 15-methyl-PGE1 [35700-26-6] (100 μg/kg twice daily, s.c.) prolonged cardiac allograft survival; however, combined treatment was most effective in increasing graft survival and in decreasing mononuclear infiltration and the occurrence of graft atherosclerosis.

L42 ANSWER 35 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:107140 HCAPLUS
DOCUMENT NUMBER: 104:107140
TITLE: The structure and metabolism of collagen and proteoglycan in normal and osteoarthritic articular cartilage
AUTHOR(S): Carney, Stephen L.; **Billingham, Michael E. J.** ; Muir, Helen
CORPORATE SOURCE: Kennedy Inst. Rheumatol., London, W6 7DW, UK
SOURCE: International Congress Series (1985), 668(Degener. Jt), 117-28
CODEN: EXMDA4; ISSN: 0531-5131
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 20 refs. The authors' recent research on proteoglycan formation, degradation, and structure in the articular cartilage of osteoarthritic stifle joints in dogs is emphasized.

L42 ANSWER 36 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:66420 HCAPLUS
DOCUMENT NUMBER: 104:66420
TITLE: Enzymic heterogeneity of normal canine articular cartilage
AUTHOR(S): Dunham, Jane; Shackleton, D. R.; Bitensky, Lucille; Chayen, J.; **Billingham, M. E. J.**; Helen Muir, I.
CORPORATE SOURCE: Div. Cell. Biol., Kennedy Inst. Rheumatol., London, W6 7DW, UK
SOURCE: Cell Biochemistry and Function (1986), 4(1), 43-6
CODEN: CBFUDH; ISSN: 0263-6484
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Articular cartilage is generally considered to be a homogeneous tissue. It has now been shown that, although different regions of the medial tibial cartilage of the dog have very similar oxidative enzymic activities, each region is heterogeneous with respect to these activities. The conventional histol. delineation of this cartilage has been modified to take into account a narrow band (designated zone 2a), just below the most superficial spindle-shaped cells, that has higher oxidative enzymic activity than any other. Changes in the activity in this zone might be diluted by the lack of change in other zones if measured by conventional biochem. procedures which could not measure the activities of the different zones sep.

L42 ANSWER 37 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:4246 HCAPLUS
DOCUMENT NUMBER: 104:4246
TITLE: Altered orientation of glycosaminoglycans and cellular changes in the tibial cartilage in the first two weeks of experimental canine osteoarthritis
AUTHOR(S): Dunham, Jane; Shackleton, D. R.; Nahir, A. M.; **Billingham, M. E. J.**; Bitensky, Lucille; Chayen, J.; Muir, I. Helen
CORPORATE SOURCE: Div. Cell. Biol., Kennedy Inst. Rheumatol., London, UK
SOURCE: Journal of Orthopaedic Research (1985), 3(3), 258-68
CODEN: JOREDR; ISSN: 0736-0266
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Changes in the cellularity and in the nature of the matrix were studied in the cartilages of the tibial plateau in exptl. induced arthritis in the dog, 7 and 14 days after section of the anterior cruciate ligament. The orientation of the glycosaminoglycans were assessed by the induced birefringence method. Only the region of the medial tibial cartilage that was unprotected by the meniscus was affected, showing increased water content, loss of superficial cells, and a decrease in orientation of the glycosaminoglycans. Whereas the birefringence of the collagen was unaffected, the superficial area that lacked oriented glycosaminglycans was markedly increased; this may be a useful indicator of early osteoarthritic changes.

L42 ANSWER 38 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:612716 HCAPLUS
DOCUMENT NUMBER: 103:212716
TITLE: Structure of newly synthesized (35S)-proteoglycans and (35S)-proteoglycan turnover products of cartilage explant cultures from dogs with experimental osteoarthritis
AUTHOR(S): Carney, Stephen L.; **Billingham, Michael E. J.** ; Muir, Helen; Sandy, John D.
CORPORATE SOURCE: Div. Biochem., Kennedy Inst. Rheumatol., London, W6 7DW, UK
SOURCE: Journal of Orthopaedic Research (1985), 3(2), 140-7
CODEN: JOREDR; ISSN: 0736-0266
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The structure of newly synthesized proteoglycans from explant cultures of cartilage from joints subjected to transection of the anterior cruciate ligament (osteoarthritic) and from normal (non- or sham-operated) joints was examined The structure of the products of proteoglycan turnover was also examined using explants of normal and osteoarthritic cartilage maintained in culture for a 48 h chase period. Newly synthesized [35S]proteoglycans extracted from cartilage explants from osteoarthritic joints, whether examined 3 wk, 3 mo, or 6 mo after surgery, were larger than those from corresponding normal cartilage. This can be explained by the synthesis in osteoarthritic cartilage of abnormally long chondroitin sulfate chains on newly synthesized proteoglycans. The exts. also contained a newly formed small proteoglycan species that was unable to interact with hyaluronic acid. The proportion of this species was higher in osteoarthritic cartilage compared with normal, examined 3 wk after surgery, but was generally absent from cartilage obtained 3 and 6 mo after surgery. Compared with controls, a smaller proportion of the [35S]proteoglycans released into the maintenance medium of explant cultures of osteoarthritic cartilage during a 48 h chase period was able to interact with hyaluronic acid. However, although furnished with longer [35S]glycosaminoglycan chains, these proteoglycans were smaller than those from control explants.

L42 ANSWER 39 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:22381 HCAPLUS
DOCUMENT NUMBER: 102:22381
TITLE: Demonstration of increased proteoglycan turnover in cartilage explants from dogs with experimental osteoarthritis
AUTHOR(S): Carney, Stephen L.; **Billingham, Michael E. J.** ; Muir, Helen; Sandy, John D.
CORPORATE SOURCE: Div. Biochem., Kennedy Inst. Rheumatol., London, W6 7DW, UK
SOURCE: Journal of Orthopaedic Research (1984), 2(3), 201-6
CODEN: JOREDR; ISSN: 0736-0266
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The turnover of proteoglycans (assessed by the release into the medium of newly synthesized [35S]proteoglycan) in explant cultures of articular cartilage from various anatomical sites of the knee joints (stifle) of mature beagles with exptl. osteoarthritis was studied. The proportion of newly synthesized proteoglycans released from cartilage explants maintained in vitro was generally increased for cartilage from operated compared and nonoperated control joints. At 3 wk after surgery there was an increase in the release of [35S]proteoglycans from explants of the lateral and medial tibial plateau of operated joints compared with sham-operated joints but not from other sites. When this comparison was made at 3-6 mo after surgery, significant increases in the release of [35S]proteoglycans were observed from cartilage of all anatomical areas except the patellar groove. The release of [35S]proteoglycan from cartilage explant cultures was dependent on live chondrocytes, since freeze-thawing the tissue immediately after labeling markedly reduced the release from both normal and osteoarthritic cartilage.

L42 ANSWER 40 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:207472 HCAPLUS
DOCUMENT NUMBER: 100:207472
TITLE: In vivo and in vitro stimulation of chondrocyte biosynthetic activity in early experimental osteoarthritis
AUTHOR(S): Sandy, John D.; Adams, Mark E.; **Billingham, Michael E. J.**; Plaas, Anna; Muir, Helen
CORPORATE SOURCE: Div. Biochem., Kennedy Inst. Rheumatol., London, UK
SOURCE: Arthritis & Rheumatism (1984), 27(4), 388-97
CODEN: ARHEAW; ISSN: 0004-3591
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The biosynthesis of proteoglycans in the menisci and articular cartilages of the knee (stifle) of mature beagles was studied in the early stages of exptl. osteoarthritis. The rate of proteoglycan synthesis, determined by systemic labeling in vivo at 21, 42, and 84 days after sectioning of the anterior cruciate ligament, was generally 1.5-2.5-fold higher than control in articular cartilages and 3-10-fold higher than control in menisci. The medial meniscus was more stimulated than the adjacent tibial area. This area-specific stimulation suggests the involvement of mech. factors in the cellular response. The rate of proteoglycan synthesis determined in vitro at 7, 14, and 21 days after operation was also about 2-fold higher than control in articular cartilages and about 3-fold higher in menisci. This increase in biosynthetic activity in vitro was confirmed by 35S-autoradiog. and appeared to be due to general stimulation of existing chondrocytes, particularly in the middle and deep zones of the articular cartilage and throughout the meniscal cartilage. The rate of proteoglycan synthesis determined in vitro in cartilages from 2-wk and 3-wk sham-operated joints was also increased relative to controls, suggesting that humoral as well as mech. factors are involved in stimulating chondrocyte activity.

L42 ANSWER 41 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:586887 HCAPLUS
DOCUMENT NUMBER: 99:186887
TITLE: Models of arthritis and the search for anti-arthritic drugs
AUTHOR(S): **Billingham, M. E. J.**
CORPORATE SOURCE: Pharm. Div., Imp. Chem. Ind. PLC, Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Pharmacology & Therapeutics (1983), 21(3), 389-428
CODEN: PHTHDT; ISSN: 0163-7258
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 192 refs.

L42 ANSWER 42 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:566567 HCAPLUS
DOCUMENT NUMBER: 95:166567
TITLE: The glycosaminoglycans (GAGs) in the menisci in an experimental osteoarthritis (OA)
AUTHOR(S): Adams, M. E.; **Billingham, M. E. J.**; Muir, Helen
CORPORATE SOURCE: Kennedy Inst. Rheumatol., London, UK
SOURCE: Seminars in Arthritis and Rheumatism (1981), 11(1, Suppl. 1), 34-5
CODEN: SAHRBF; ISSN: 0049-0172
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Different regions of normal dog (foxhound and beagle) knee menisci showed similar proportions of GAG fractions: 60% chondroitin-6-sulfate; 25% chondroitin-4-sulfate; 10% unsulfated chondroitin; 5% dermatan sulfate, and 6-7% hyaluronic acid. Knees of foxhounds with natural OA had increased chondroitin-6-sulfate in the central portion of the medial meniscus, and increased hyaluronic acid in the lateral meniscus. In exptl. OA in beagles (anterior cruciate ligament of 1 knee was severed by a stab incision), uronic acid and galactosamine decreased initially, but rose above normal from 3 mo onwards. However, the glucosamine content was decreased, particularly in the medial meniscus, for as long as 15 mo, suggesting a decreased keratin sulfate content. Thus, changes in the menisci of the severely affected foxhound joint differed somewhat from those of menisci from operated beagle joints. The sequential changes in the meniscus in this exptl. model of osteoarthrosis are not exactly the same as those seen in cartilage, suggesting that some repair of the meniscus does occur.

L42 ANSWER 43 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:566566 HCAPLUS
DOCUMENT NUMBER: 95:166566
TITLE: In vivo metabolism of proteoglycans in experimental osteoarthritic and normal canine articular cartilage and the intervertebral disk
AUTHOR(S): McDevitt, Cahir A.; **Billingham, Michael E. J.** ; Muir, Helen
CORPORATE SOURCE: Kennedy Inst. Rheumatol., London, UK
SOURCE: Seminars in Arthritis and Rheumatism (1981), 11(1, Suppl. 1), 17-18
CODEN: SAHRBF; ISSN: 0049-0172
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Proteoglycans of the intervertebral disks were synthesized as large mols. with functional hyaluronate-binding sites; they are gradually converted to small nonaggregating mols. in the extracellular matrix. Hyaline cartilage proteoglycans, in contrast, appear to be enzymically cleaved at the distal end of the protein cone to yield smaller mols. with intact hyaluronate-binding sites. In exptl. osteoarthritic cartilage, the total proteoglycan activities were higher than controls, and there was a higher rate of proteoglycan deposition in the extracellular matrix. Proteoglycans of both lesion sites and adjacent intact cartilage had decreased half-lives; the rate of proteoglycan removal from the extracellular matrix of the osteoarthritic cartilage was increased as compared to controls.

L42 ANSWER 44 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:583924 HCAPLUS
DOCUMENT NUMBER: 93:183924
TITLE: Biosynthesis of collagen and other matrix proteins by articular cartilage in experimental osteoarthrosis
AUTHOR(S): Eyre, David R.; McDevitt, Cahir A.; **Billingham, Michael E. J.**; Muir, Helen
CORPORATE SOURCE: Dep. Biol. Chem., Child. Hosp. Med. Cent., Boston, MA, 02115, USA
SOURCE: Biochemical Journal (1980), 188(3), 823-37
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In dogs with surgically-induced osteoarthrosis of one knee joint, collagen formation was stimulated in all cartilage surfaces at 2, 8, and 24 wk after surgery. Systemic labeling with proline-3H showed that >10-fold more collagen was deposited per dry weight of exptl. cartilage compared with control cartilage in unoperated knee. Type II collagen was the radiolabeled product in all samples of exptl. cartilage ranging in quality from undamaged to overtly fibrillated. In exptl. knees the new collagen was less glycosylated than in controls. However, no difference in glycosylation of the total collagen in the tissues was observed by chemical anal. Of the protein-bound 3H, >50 and ≤25% was extracted by 4M guanidinium chloride from control and exptl. cartilage resp. Two-thirds of the extracted 3H separated in the upper fraction on d.-gradient centrifugation in CsCl under associative conditions; much of this ran as a single protein band on SDS-polyacrylamide gel electrophoresis under reducing conditions. The identity of this protein was unknown, but it resembled serum albumin in mobility after disulfide bond cleavage.

L42 ANSWER 45 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:121735 HCAPLUS
DOCUMENT NUMBER: 92:121735
TITLE: Correlation between the rise in acute phase proteins and histological evidence of ulceration in the rat following indomethacin treatment
AUTHOR(S): **Billingham, M. E. J.**; Tucker, Mary J.
CORPORATE SOURCE: Dep. Biol., ICI Pharm. Div., Macclesfield, UK
SOURCE: British Journal of Pharmacology (1979), 67(3), 450P-451P
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In rats fasted for 12 h and then given indomethacin [53-86-1] (5-20 mg/kg, orally), the increase in plasma α-glycoprotein was correlated with the severity of gastrointestinal damage produced by indomethacin, as determined histol. and in body weight changes. Thus, plasma α-glycoprotein levels may be a useful means of following, noninvasively, the time course of the ulcerative process.

L42 ANSWER 46 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:488909 HCAPLUS
DOCUMENT NUMBER: 91:88909
TITLE: Pregnancy-associated α2-glycoprotein (α2-PAG) and various acute phase reactants in rheumatoid arthritis and osteoarthritis
AUTHOR(S): Horne, C. H. W.; Thomson, A. W.; Hunter, Christine B. J.; Tunstall, Anita M.; Towler, C. M.; **Billingham, M. E. J.**
CORPORATE SOURCE: Dep. Pathol., Univ. Aberdeen Foresterhill, Aberdeen, UK
SOURCE: Biomedicine (Paris, France) (1979), 30(2), 90-4
CODEN: BIMDB3; ISSN: 0300-0893
DOCUMENT TYPE: Journal
LANGUAGE: English
AB α2-PAG concns. were measured in matched serums and synovial fluid samples obtained from 36 patients with rheumatoid arthritis and 10 patients with osteoarthritis. Levels of α2-PAG in serum and synovial fluid were significantly higher in rheumatoid arthritis than in osteoarthritis. Calcn. of the synovial fluid/serum ratios for α2-PAG gave results which were explicable only if this protein were being synthesized locally. In a longitudinal study of 15 patients with rheumatoid arthritis, concns. of α2-PAG did not reflect disease activity, unlike those of the classical acute phase reactants, C-reactive protein and ceruloplasmin.

L42 ANSWER 47 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:161767 HCAPLUS
DOCUMENT NUMBER: 90:161767
TITLE: Experimental models of arthritis in animals as screening tests for drugs to treat arthritis in man
AUTHOR(S): **Billingham, M. E. J.**; Davies, G. E.
CORPORATE SOURCE: ICI Ltd., Macclesfield/Cheshire, UK
SOURCE: Handbook of Experimental Pharmacology (1979), 50(2; Anti-Inflammatory Drugs), 108-44
CODEN: HEPHD2; ISSN: 0171-2004
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with .apprx.200 refs.

L42 ANSWER 48 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:470642 HCAPLUS
DOCUMENT NUMBER: 89:70642
TITLE: Anthracycline cardiomyopathy monitored by morphologic changes
AUTHOR(S): **Billingham, M. E.**; Mason, J. W.; Bristow, M. R.; Daniels, J. R.
CORPORATE SOURCE: Dep. Pathol., Stanford Univ. Med. Cent., Stanford, CA, USA
SOURCE: Cancer Treatment Reports (1978), 62(6), 865-72
CODEN: CTRRDO; ISSN: 0361-5960
DOCUMENT TYPE: Journal
LANGUAGE: English
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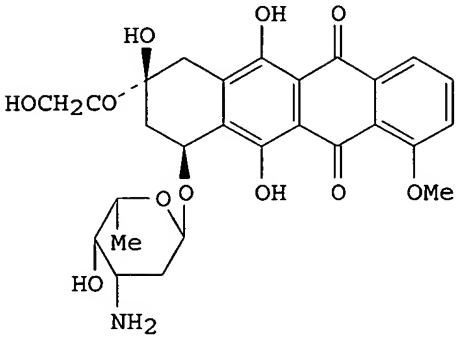

I

AB Seventy-six endomyocardial biopsies obtained from 60 patients receiving Adriamycin (I) [23214-92-8] and other anthracycline analogs were studied. The biopsies were studied by light and electron microscopy. Two main types of myocyte degeneration were consistently present; the lesions were focal, and inflammatory infiltrate was absent. The severity of pathologic changes was graded on a scale from 0 (normal) to 3 (marked abnormality). Twelve patients receiving previous mediastinal irradiation (600-5700 rads) showed a mean pathol. grade (2.0) that was higher than in those patients receiving a comparable dose of I but who were not irradiated (1.18). Radiation, even if remote, enhances I-induced cardiotoxicity and evokes a "recall" phenomenon of latent, acute irradiation changes. A specific, progressive, subclin. injury to the heart occurs with anthracycline therapay that cannot be detected reliably by conventional tests. Anthracycline-induced cardiotoxicity in rabbits, monkeys, and dogs shows the same basic cellular lesions as in man. The analogs, adria-DNA and rubidiazone [54083-22-6], also show lesions similar to those produced by I in the human heart. The endomyocardial biopsy is a reliable method for monitoring cardiac damage due to anthracyclines in man.

L42 ANSWER 49 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:419953 HCAPLUS
DOCUMENT NUMBER: 87:19953
TITLE: The role of the acute phase reaction in inflammation
AUTHOR(S): **Billingham, M. E. J.**; Gordon, A. H.
CORPORATE SOURCE: Natl. Inst. Med. Res., London, UK
SOURCE: Future Trends Inflammation, Proc. Int. Meet., 2nd (1975), 195-200. Editor(s): Giroud, Jean Pierre; Willoughby, D. A.; Velo, G. P. Birkhaeuser: Basel, Switz.
CODEN: 35PYAL
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The changes in concentration and synthesis rate of albumin, fibrinogen, and α1 acid glycoprotein during adjuvant arthritis were examined in the rat. The changes which occur are regulated at the liver by alteration of the rate of synthesis of the individual protein. For example albumin at the height of adjuvant arthritis falls to 3% of its normal plasma level whereas the level of α1 acid glycoprotein increases up to 20-fold; these changes are reflected by similar changes in their synthesis rate by the liver. The effect of the fall in albumin concentration on the plasma binding of anti-inflammatory drugs (and their toxicity) in relation to these findings were discussed along with the biol. role of the acute phase plasma proteins and hence the influence of the liver in the response to injury.

L42 ANSWER 50 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:507132 HCAPLUS
DOCUMENT NUMBER: 85:107132
TITLE: Changes in concentration and synthesis rates of plasma proteins during experimental arthritis
AUTHOR(S): **Billingham, M. E. J.**; Gordon, A. H.
CORPORATE SOURCE: Natl. Inst. Med. Res., London, UK
SOURCE: Protides of the Biological Fluids (1976), Volume Date 1975, 23, 451-4
CODEN: PBFPA6; ISSN: 0079-7065
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The formation of fibrinogen, α1-acid and α2-glycoproteins, and albumin in liver, and their levels in blood plasma, were monitored in male rats with exptl. induced arthritis. Plasma levels of fibrinogen, and α1-acid, and α2-glycoproteins increased and that of albumin decreased, as the degree of arthritic inflammation increased. Albumin levels decreased to <50% of normal on day 20, while α1-acid glycoprotein was up to 15-fold greater than normal. Fibrinogen formation was 3-fold greater at the height of arthritis (day 18-20).

L42 ANSWER 51 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:418368 HCAPLUS
DOCUMENT NUMBER: 85:18368
TITLE: The role of the acute phase reaction in inflammation
AUTHOR(S): **Billingham, M. E. J.**; Gordon, A. H.
CORPORATE SOURCE: Natl. Inst. Med. Res., London, UK
SOURCE: Agents and Actions (1976), 6(1-3), 195-200
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A study is described of the change in the circulating levels of plasma proteins (albumin, fibrinogen, and α1-acid glycoprotein) that occurs after inflammatory injury (adjuvant arthritis) and the manner in which these changes in plasma concentration are controlled by changes in the rate of synthesis. The changes that occur are regulated at the liver by alteration of the rate of synthesis of the individual proteins. For example albumin at the height of adjuvant arthritis falls to 33% of its normal plasma level, whereas the level of α1-acid glycoprotein increases up to 20-fold; these changes are reflected by similar changes in their synthesis rate by the liver. The effect of the fall in albumin concentration on the plasma binding of anti-inflammatory drugs (and their toxicity) in relation to these findings is discussed, along with the biol. role of the acute phase plasma proteins and, hence, the influence of the liver in the response to injury.

L42 ANSWER 52 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:128997 HCAPLUS
DOCUMENT NUMBER: 80:128997
TITLE: Antiinflammatory peptide from bee venom
AUTHOR(S): **Billingham, M. E. J.**; Morley, J.; Hanson, Jennifer M.; Shipolini, R. A.; Vernon, C. A.
CORPORATE SOURCE: Dep. Pharmacol., Guy's Hosp. Med. Sch., London, UK
SOURCE: Nature (London, United Kingdom) (1973), 245(5421), 163-4
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptide 401 (I) [32908-73-9] from bee venom contained 22 residues in a sequence identical to a mast cell degranulating peptide isolated by H. Briethaupt and E. Habermann (1968), and had inflammatory activity at very low concns. (1-1000 ng/kg, intradermal) but antiinflammatory activity (100 times greater than hydrocortisone) at higher concns. (200 μg/kg, i.v. or 1 mg/kg, s.c.) that was independent of the mast cell lyzing activity. Mepyramine [91-84-9] (2.5 mg/kg) or methysergide [361-37-5] (2.5 mg/kg) inhibited the inflammatory but not the antiinflammatory activity of I. Inflammation associated with the primary and secondary lesions in adjuvant-induced arthritis in rats was reduced by I and, if injected with the adjuvant (Mycobacterium tuberculosis) I inhibited development of the disease.

L42 ANSWER 53 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1972:401374 HCAPLUS
DOCUMENT NUMBER: 77:1374
TITLE: Separation of irritancy from the antiinflammatory component of inflammation exudate
AUTHOR(S): **Billingham, M. E. J.**; Robinson, B. V.
CORPORATE SOURCE: Dep. Biophys., Natl. Inst. Med. Res., London, UK
SOURCE: British Journal of Pharmacology (1972), 44(2), 317-20
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antiinflammatory activity of rat inflammation exudates was separated from the irritant factor of crude exudates by Sephadex gel filtration and polyacrylamide electrophoresis. Therefore, the irritancy of the unpurified preparation was apparently due to substances (enzymes or cell breakdown products) in the exudate other than the antiinflammatory protein. This separation of activities refuted the explanation of the action of the antiinflammatory exudate in terms of a nonspecific counter-irritation of unknown mechanism.

L42 ANSWER 54 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1971:417452 HCAPLUS
DOCUMENT NUMBER: 75:17452
TITLE: Role of the liver in inflammation
AUTHOR(S): **Billingham, M. E. J.**; Gordon, Arthur Hugh; Robinson, Bryan V.
CORPORATE SOURCE: Natl. Inst. Med. Res., London, UK
SOURCE: Nature (London), New Biology (1971), 231(18), 26-7
CODEN: NNBYA7; ISSN: 0369-4887
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The inhibition of carrageenin-induced edema of the rat hind paw was attributed to an antiinflammatory protein which was separated from plasma previously used for perfusion of livers from injured (inflammation) rats. Actinomycin D (100 μg/kg) injected i.p. into rats 2 hr before injury and 24, 48, and 72 hr after injury inhibited the appearance of the antiinflammatory protein, indicating de novo synthesis of the plasma protein following inflammation injury.

L42 ANSWER 55 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1971:40396 HCAPLUS
DOCUMENT NUMBER: 74:40396
TITLE: Partial purification of antiinflammatory factor(s) found during experimental and clinical inflammation
AUTHOR(S): **Billingham, M. E. J.**; Robinson, Bryan V.; Robson, John Michael
CORPORATE SOURCE: Med. Sch., Guy's Hosp., London, UK
SOURCE: Inflammation Biochem. Drug Interaction, Proc. Int. Symp. (1969), Meeting Date 1968, 204-9. Editor(s): Bertelli, A. Excerpta Med.: Amsterdam, Neth.
CODEN: 22NQAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Purification yielded antiinflammatory factor with >3 times the original activity; the material was 30-fold purified, but not homogeneous and appeared as 4 bands on starch gel electrophoresis and .apprx.10 bands on acrylamide gel electrophoresis. The substance may originate at the site of inflammation or at a different site such as the liver. The substance was not a steroid, but protein in nature, and had a limiting function in the progress of the inflammatory reaction.

L42 ANSWER 56 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:401921 HCAPLUS
DOCUMENT NUMBER: 71:1921
TITLE: Partial purification of the anti-inflammatory factor(s) in inflammatory exudate
AUTHOR(S): **Billingham, M. E. J.**; Robinson, Bryan V.; Robson, J. M.
CORPORATE SOURCE: Guy's Hosp. Med. Sch., London, UK
SOURCE: British Journal of Pharmacology (1969), 35(3), 543-57
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The carrageenin foot test was established as a sensitive and reliable assay procedure for determining the antiinflammatory activity of inflammatory exudates. Incubation alone at a temperature above 70° or with pronase at 37° destroyed the antiinflammatory activity of exudate. The antiinflammatory component of exudate was partially precipitated by 50% (NH4)2SO4. A partial purification process was devised using Sephadex G-150 gel filtration and DEAE-and CM-cellulose ion-exchange chromatog. to obtain at least a 24-fold purification. Measurements of 11-hydroxy corticosteroid levels indicated that steroids were not involved in the mechanism by which the exudate produced its antiinflammatory effects.

L42 ANSWER 57 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:56490 HCAPLUS
DOCUMENT NUMBER: 68:56490
TITLE: Factorial design in undergraduate organic experiments
AUTHOR(S): Smith, Robert Bruce; **Billingham, Edward J., Jr.**
CORPORATE SOURCE: Nevada Southern Univ., Las Vegas, NV, USA
SOURCE: Journal of Chemical Education (1968), 45(2), 113-15
CODEN: JCEDA8; ISSN: 0021-9584
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Friedel-Crafts butylation of C6H6 was used to study the effects of varying reaction conditions on absolute yield of a reaction product. Three temperature levels (25, 50, and 80°) and 2 molar ratios of AlCl3 to 2-bromobutane (1:5 and 1:25) were used. The isomer distribution in each product was determined by ir anal. Factorial anal. was applied to reach conclusions concerning the effects on product distribution exerted by temperature and catalyst proportion. The reliability of the conclusions was evaluated by statistical anal. Fisher's t-test was applied to the data to determine whether there were significant differences between the results of various treatments. The student results obtained agreed reasonably well with those reported by Roberts and by Dunathan. 11 references.

L42 ANSWER 58 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1964:414700 HCAPLUS
DOCUMENT NUMBER: 61:14700
ORIGINAL REFERENCE NO.: 61:2467e
TITLE: Thermometric determination of copper by iodometry
AUTHOR(S): **Billingham, E. J., Jr.**; Reed, Allan H.
CORPORATE SOURCE: Thiel Coll., Greenville, PA
SOURCE: Anal. Chem. (1964), 36(6), 1148-9
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. Jordan and Alleman, CA 51, 6423f. The equivalence point in iodometric titration of Cu(II) may be determined thermometrically. Accuracy is better than 3%.

L42 ANSWER 59 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:472521 HCAPLUS
DOCUMENT NUMBER: 57:72521
ORIGINAL REFERENCE NO.: 57:14424c-f
TITLE: Kinetically differentiated enthalpy titration curves
AUTHOR(S): Jordan, Joseph; **Billingham, E. J., Jr.**
CORPORATE SOURCE: Pennsylvania State Univ., University Park
SOURCE: U.S. At. Energy Comm. (1960), Volume NYO-2215, 21 pp.
From: Nucl. Sci. Abstr. 14, Abstr. No. 12589 (1960).
DOCUMENT TYPE: Report
LANGUAGE: Unavailable

AB When a soluble oxalate was titrated rapidly into a dilute solution of Ca in a pH 8
borate buffer, a well-defined thermometric-titration curve was obtained, corresponding to instantaneous exothermic precipitation of CaC2O4. In contradistinction, the analogous titration curve of Mg with C2O4-- was quasi-isothermal in shape because of a slow precipitation mechanism involving a complex intermediate. Based on these differences in kinetic behavior, a method was developed for the determination of Ca in the presence of Mg. The procedure involves an automatic thermometric titration with standard C2O4--, and was adapted to the nonsep. analysis of Ca in limestone and dolomite. It combines the advantages of a macrosample and a micro-titration.

L42 ANSWER 60 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:110699 HCAPLUS
DOCUMENT NUMBER: 55:110699
ORIGINAL REFERENCE NO.: 55:20755i,20756a
TITLE: Thermochemical titrations in fused salts
AUTHOR(S): Jordan, Joseph; Meier, Jurg; **Billingham, Edward J., Jr.**; Pendergrast, James
CORPORATE SOURCE: Pennsylvania State Univ., University Park
SOURCE: Anal. Chem. (1960), 32, 651-5
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Cl- is determined in a molten alkali nitrate eutectic by thermometric precipitation
titration with AgNO3 at 150-200° in an adiabatic cell in which temperature fluctuations are reduced to ±0.0005°. For concns. between 8 + 10-4 and 2 + 10-2M, the temperature change during titration is measured with a thermistor bridge. This method is also applicable to rapid determination of heats of reaction in fused salts under isothermal conditions.

L42 ANSWER 61 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:36987 HCAPLUS
DOCUMENT NUMBER: 55:36987
ORIGINAL REFERENCE NO.: 55:7157f-i
TITLE: Thermometric precipitation titration of calcium in the presence of magnesium. Kinetic masking and application to limestone analysis
AUTHOR(S): Jordan, Joseph; **Billingham, E. J., Jr.**
CORPORATE SOURCE: Pennsylvania State Univ., University Park
SOURCE: Anal. Chem. (1961), 33, 120-3
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB When a soluble oxalate (0.2M NH4 oxalate) was titrated rapidly into a dilute solution (0.01M) of Ca in a pH 8 borate buffer, a well-defined thermometric titration curve was obtained, corresponding to instantaneous exothermic precipitation of Ca oxalate. In contradistinction, the analogous titration curve of 0.01M Mg with oxalate was quasi-isothermal in shape because of a slow precipitation mechanism involving a complex intermediate. A method for the determination of Ca in the presence of Mg was based on these differences in kinetic behavior. It is rapid and combines the convenience of using a macrosample with the advantage of a microprocedure. A 1-2-g. sample was dried for 1 hr. at 110° and dissolved in 15 ml. of 6M HCl. The solution was evaporated to dryness, and the residue heated to 110° for 30 min. Then, 25 ml. of 3M HCl was added, and any insol. residue was filtered off and washed with 5 20-ml. portions of 1% HCl. The washings were then added to the filtrate, which was then reduced to 10 ml. on a hot plate and cooled, the pH was adjusted to 4-6 by the addition of M NaOH. A precipitate of hydrous oxides, mainly of Fe and Al, may form at this point. The solution (20-50 ml. in volume) was made up to 500 ml. by diluting with pH 8 borate buffer (0.005M in total borate). The precipitate was allowed to settle, and aliquots of supernatant liquid were pipetted off and used for titrating. In each experiment, 50 ml. of solution was titrated with 0.2M NH4 oxalate titrant. The initial temperature of the titrant and test solns. was controlled to ±0.2°, and all test solns. were buffered at pH 8. 21 references.

L42 ANSWER 62 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:576 HCAPLUS
DOCUMENT NUMBER: 55:576
ORIGINAL REFERENCE NO.: 55:90b-d
TITLE: Enthalpy titrations and thermochemistry in molten salts
AUTHOR(S): Jordan, Joseph; Meier, Jurg; **Billingham, Edward J., Jr.**; Pendergrast, James
CORPORATE SOURCE: Pennsylvania State Univ., University Park, PA
SOURCE: Nature (London, United Kingdom) (1960), 187, 318-19
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 53, 21366b. The results of thermometric titrations with AgNO3 of KCl, KBr, KI, and K2CrO4 in fused LiNO3-KNO3 at 431°K. are summarized. The temperature change (0.01-0.5°) in the titrated melt was monitored by a thermistor bridge. The titrant was delivered by remote control to a special adiabatic cell in a supernatant argon atmospheric The plot for titration of K2CrO4 is given. Data inferred from the titration curves include the stoichiometry of the reaction, the heat of the titration reaction, ΔH°, the solubility-product constant and the corresponding free energy, ΔF°, of precipitation, and the entropy, ΔS°, of the reaction. The entropy of precipitation of the Ag halides was normal, whereas the precipitation of Ag2CrO4 was anentropic.

L42 ANSWER 63 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1959:119820 HCAPLUS
DOCUMENT NUMBER: 53:119820
ORIGINAL REFERENCE NO.: 53:21366b-c
TITLE: Thermometric titration in fused salts
AUTHOR(S): Jordan, Joseph; Meier, Jurg; **Billingham, E. J., Jr.**; Pendergrast, James
CORPORATE SOURCE: Pennsylvania State Univ., Univ. Park, PA
SOURCE: Anal. Chem. (1959), 31, 1439-40
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The argentometric determination of chloride by continuous thermometric titration
in a fused LiNO3-KNO3 eutectic melt is described. The effective mean accuracy range of the detns. was between 1 and 2%.

L42 ANSWER 64 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1922:18811 HCAPLUS
DOCUMENT NUMBER: 16:18811
ORIGINAL REFERENCE NO.: 16:3207f
TITLE: Disintegrating paper stock by impinging streams
INVENTOR(S): **Billingham, M. C. J.**
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 1422251		19220711	US 1918-246695	19180725

AB Unavailable

L42 ANSWER 65 OF 65 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1922:17371 HCAPLUS
DOCUMENT NUMBER: 16:17371
ORIGINAL REFERENCE NO.: 16:2990c
TITLE: Apparatus for disintegrating and de-inking paper-stock
INVENTOR(S): **Billingham, M. C. J.**
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 1420362		19220620	US 1920-407468	19200901

AB The printed stock is injected upwardly through a vertical nozzle against a perforated baffle which effects disintegration.

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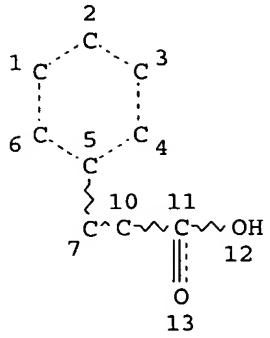


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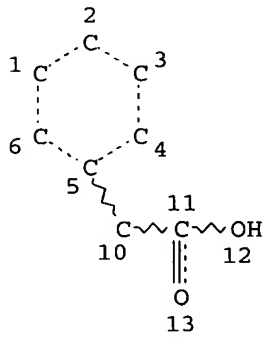


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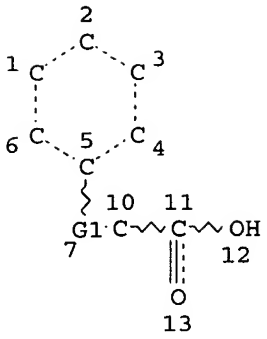

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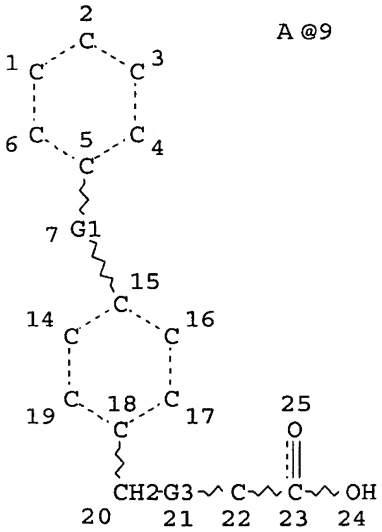

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DEFAULT ECLEVEL IS LIMITED

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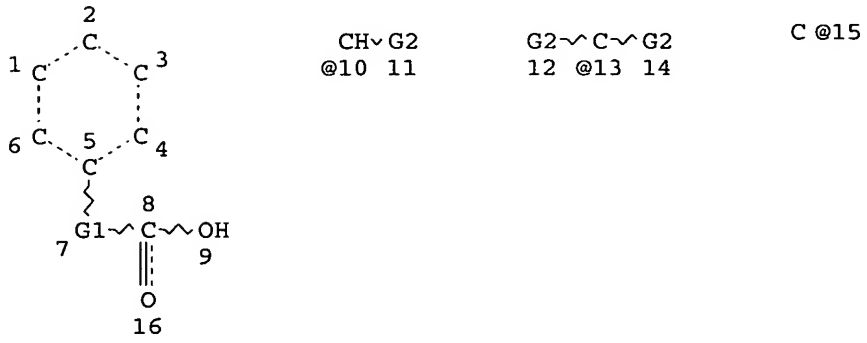

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STEREO ATTRIBUTES: NONE

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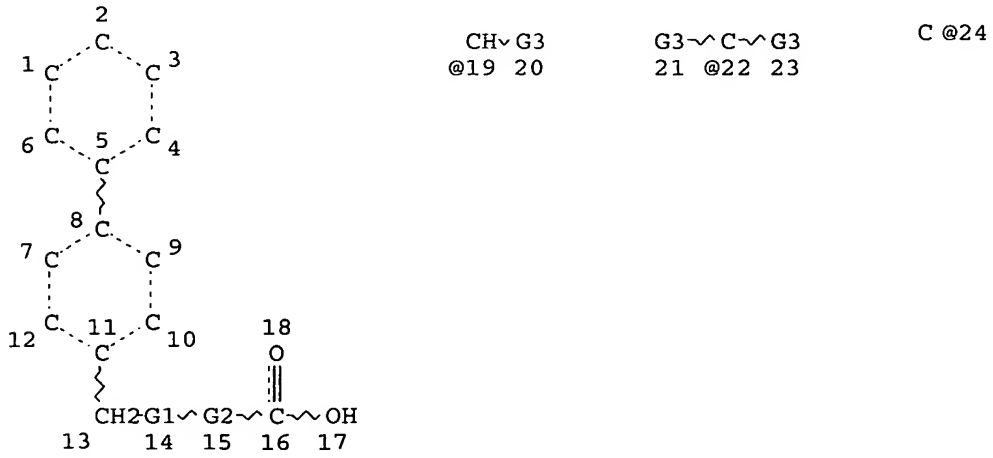

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DEFAULT MLEVEL IS ATOM
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STEREO ATTRIBUTES: NONE
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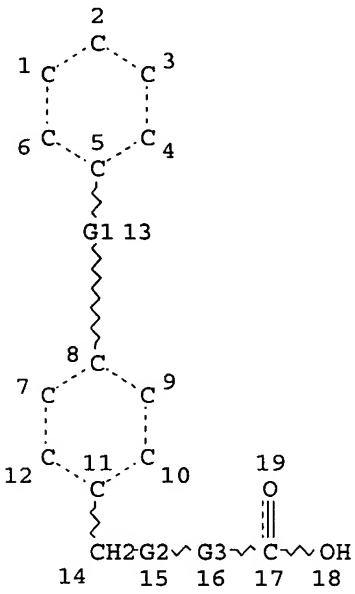

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NSPEC IS R AT 25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE
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L48 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:538255 HCAPLUS
DOCUMENT NUMBER: 135:132768
TITLE: Computational methods for generation of synthetic ligands based on the three dimensional structure of thyroid hormone receptor
INVENTOR(S): Scanlan, Thomas S.; Baxter, John D.; Fletterick, Robert J.; Wagner, Richard L.; Kushner, Peter J.; Apriletti, James J.; West, Brian L.; Shiau, Andrew K.
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: U.S., 268 pp., Cont.-in-part of U.S. 6,236,946.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6266622	B1	20010724	US 1997-980115	19971126
CA 2240024	AA	19970619	CA 1996-2240024	19961213 <--
US 6236946	B1	20010522	US 1996-764870	19961213
CA 2314096	AA	19990603	CA 1998-2314096	19981125
WO 9926966	A2	19990603	WO 1998-US25296	19981125
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9917999	A1	19990615	AU 1999-17999	19981125
AU 763452	B2	20030724		
EP 1034184	A2	20000913	EP 1998-962849	19981125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
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BR 9815061	A	20011120	BR 1998-15061	19981125
JP 2001524489	T2	20011204	JP 2000-522122	19981125
AU 2003220708	A1	20030814	AU 2003-220708	20030710

PRIORITY APPLN. INFO.:

US 1995-8540P	P	19951213
US 1995-8543P	P	19951213
US 1995-8606P	P	19951214
US 1996-764870	A2	19961213
US 1997-980115	A	19971126
WO 1998-US25296	W	19981125
AU 2000-34045	A3	20000511

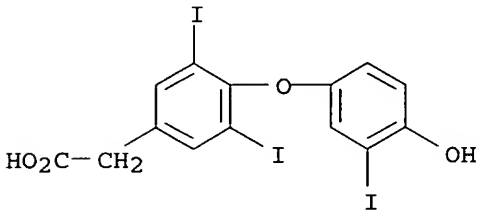
OTHER SOURCE(S): MARPAT 135:132768
AB The present invention provides new methods, particularly computational methods, and compns. for the generation of nuclear receptor synthetic ligands based on the three dimensional structure of nuclear receptors, particularly the thyroid receptor (TR). Also provided are crystals, nuclear receptor synthetic ligands, and related methods. The present invention provides for crystals of TR ligand binding domains with a ligand bound to the ligand binding domain (LBD), which provide excellent atomic resolution of the amino acids that interact with TR ligand, especially thyroid receptor ligands. The three dimensional model of a TR LBD with a ligand bound reveals a previously unknown structure for nuclear receptors and

shows that the ligand is bound in a water inaccessible binding cavity of the ligand binding domain of the TR. The present invention also includes a method for identifying a compound capable of selectively modulating the activity of a TR isoform. Further included is a method for identifying agonist or antagonist ligands of a TR using the atomic coordinates of a LBD in conjunction with a computerized modeling system. Also provided is a method of identifying a compound that selectively modulates the activity of one type of nuclear receptor compared to other nuclear hormone receptors. Another aspect of the invention is a method for increasing the receptor selectivity of a compound for a particular type of nuclear receptor. The invention finds use in the selection and characterization of peptide, peptidomimetic or synthetic compds. identified by the methods of the invention, particularly new lead compds. useful in treating disorders related to nuclear receptor-based deficiencies, including TR-related disorders.

IT **51-24-1**, triac
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(complexed with TR-β; computational methods for generation of synthetic ligands based on three dimensional structure of **thyroid hormone receptor**)

RN 51-24-1 HCAPLUS

CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



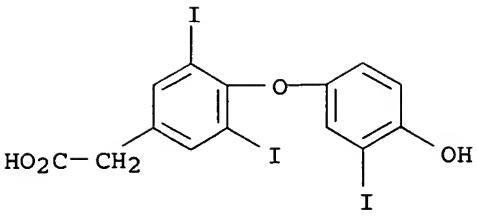
REFERENCE COUNT: 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:266770 HCAPLUS
DOCUMENT NUMBER: 131:68221
TITLE: Acute Effects of Thyroid Hormone Analogs on Sodium Currents in Neonatal Rat Myocytes
AUTHOR(S): Huang, Chien-Jung; Geller, Herbert M.; Green, William L.; Craelius, William
CORPORATE SOURCE: Department of Biomedical Engineering, Rutgers University, Piscataway, NJ, 08854, USA
SOURCE: Journal of Molecular and Cellular Cardiology (**1999**), 31(4), 881-893
CODEN: JMCDAY; ISSN: 0022-2828
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

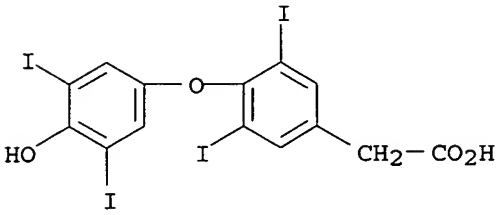
AB The authors previously reported that T3 (3,3',5-triiodo-L-thyronine) acutely increases sodium currents (INa) in neonatal rat myocytes. Here the authors compare the effects of several thyroid hormone analogs, including T4 (3,3',5,5'-tetraiodo-L-thyronine), rT3 (3,3',5'-triiodo-L-thyronine), D-T3 (3,3',5-triiodo-D-thyronine), 3,5-T2 (3,5-diiodo-L-thyronine), DIT (3,5-diiodo-L-tyrosine), MIT (3-monoiodo-L-tyrosine), tetrac (3,3',5,5'-tetraiodo-thyroacetic acid), triac (3,3',5-triiodo-thyroacetic acid), and tyrosine, on INain cultured neonatal rat myocytes (n ranged from 9 to 28 for each comparison). T4, T3, 3,5-T2, and DIT (10 n m) all increased c.d. relative to control to a similar degree: to 1.22±0.2, 1.21±0.03, 1.16±0.02 and 1.16±0.03, resp., P<0.05. In contrast, thyroid hormone analogs with an altered side group of the inner iodophenyl ring, including tetrac, triac, and D-T3, had no effect on INa nor did rT3, MIT or tyrosine. Pretreatment with rT3 inhibited the effects of T4, T3, 3,5-T2, and DIT. Conversely, the dose-dependent inhibitory effect of amiodarone, an iodinated benzofuran derivative that antagonizes thyroid hormone actions, on INa was blocked when myocytes were pretreated with T3 (100 n m, n=3), suggesting an interaction of T3 with amiodarone. The enhancement of INa by T3and 3,5-T2 could not be blocked by propranolol, suggesting that the effects are not mediated through β-adrenergic signaling pathways. In conclusion, the present results suggest that the acute effects of thyroid hormone and analogs on cardiac INa are mediated by a non-genomic thyroid hormone receptor with a unique structure-activity relationship. (c) 1999 Academic Press.

IT **51-24-1**, 3,3',5-Triiodo-thyroacetic acid **67-30-1**, 3,3',5,5'-Tetraiodo-thyroacetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(thyroid hormone analogs acute effects on sodium currents in neonatal rat cardiac myocytes are mediated by non-genomic **thyroid hormone receptor** with unique structure-activity relationship)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



RN 67-30-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

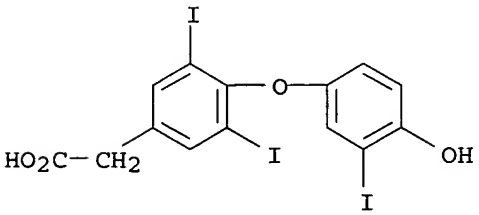


REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:180896 HCAPLUS
DOCUMENT NUMBER: 130:321080
TITLE: Thyroid hormone receptor-associated proteins and general positive cofactors mediate thyroid hormone receptor function in the absence of the TATA box-binding protein-associated factors of TFIID
AUTHOR(S): Fondell, Joseph D.; Guermah, Mohamed; Malik, Sohail; Roeder, Robert G.
CORPORATE SOURCE: Laboratory of Biochemistry and Molecular Biology, The Rockefeller University, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1999**), 96(5), 1959-1964
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Coactivators previously implicated in ligand-dependent activation functions by thyroid hormone receptor (TR) include p300 and CREB-binding protein (CBP), the steroid receptor coactivator-1 (SRC-1)-related family of proteins, and the multicomponent TR-associated protein (TRAP) complex. Here we show that two pos. cofactors (PC2 and PC4) derived from the upstream stimulatory activity (USA) cofactor fraction act synergistically to mediate thyroid hormone (T3)-dependent activation either by TR or by a TR-TRAP complex in an in vitro system reconstituted with purified factors and DNA templates. Significantly, the TRAP-mediated enhancement of activation by TR does not require the TATA box-binding protein-associated factors of TFIID. Furthermore, neither the pleiotropic coactivators CBP and p300 nor members of the SRC-1 family were detected in either the TR-TRAP complex or the other components of the in vitro assay system. These results show that activation by TR at the level of naked DNA templates is enhanced by cooperative functions of the TRAP coactivators and the general coactivators PC2 and PC4, and they further indicate a potential functional redundancy between TRAPs and TATA box-binding protein-associated factors in TFIID. In conjunction with earlier studies on other nuclear receptor-interacting cofactors, the present study also suggests a multistep pathway, involving distinct sets of cofactors, for activation of hormone responsive genes.

IT **51-24-1**, TRIAC
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**thyroid hormone receptor**-associated proteins and general pos. cofactors mediate **thyroid hormone receptor** function and signaling therein)
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:682082 HCAPLUS
DOCUMENT NUMBER: 129:285988
TITLE: Non-steroidal anti-inflammatory agents inhibition of fibrotic response to an implanted device
INVENTOR(S): Lanza, Robert P.; Chick, William L.
PATENT ASSIGNEE(S): Biohybrid Technologies, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

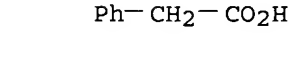
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843554	A1	19981008	WO 1998-US6062	19980327 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5891477	A	19990406	US 1997-828327	19970328 <--
AU 9867806	A1	19981022	AU 1998-67806	19980327 <--
EP 1033947	A1	20000913	EP 1998-913196	19980327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001519692	T2	20011023	JP 1998-541834	19980327

PRIORITY APPLN. INFO.:
US 1997-828327 A2 19970328
WO 1998-US6062 W 19980327

AB Methods for inhibition of fibrotic rejection of implanted devices comprising administering an effective amount of a non-steroidal anti-inflammatory agent. Composite microcapsules (alginate-polylysine) containing discordant bovine and porcine islets were implanted into the peritoneum of normal adult dogs for periods of two weeks to two months. Naproxen was orally administered at a dosage of mg/kg/day, then the dogs were sacrificed at the end of the period. The external surfaces of implanted microspheres in the naproxen-treated dogs were free of fibrosis and host cell adherence, whereas the majority of the microspheres in the untreated animals were encapsulated by thick layers of organized granulation tissue.

IT **103-82-2D**, Phenylacetic acid, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-steroidal anti-inflammatory agents inhibition of **fibrotic** response to implanted device)

RN 103-82-2 HCAPLUS
CN Benzeneacetic acid (9CI) (CA INDEX NAME)



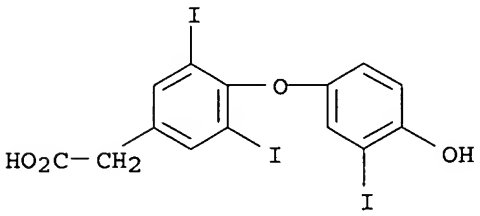
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:10607 HCAPLUS
DOCUMENT NUMBER: 124:46213
TITLE: Unliganded thyroid hormone receptor α can target TATA-binding protein for transcriptional repression
AUTHOR(S): Fondell, Joseph D.; Brunel, Franck; Hisatake, Koji; Roeder, Robert G.
CORPORATE SOURCE: Lab. Biochem. Mol. Biol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Molecular and Cellular Biology (**1996**), 16(1), 281-7
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Unliganded human thyroid hormone receptor α (hTRα) can repress transcription by inhibiting the formation of a functional preinitiation complex (PIC) on promoters bearing thyroid hormone receptor (TR)-binding elements. Here the authors demonstrate that hTRα directly contacts the TATA-binding protein (TBP) and that preincubation of hTRα with TBP completely alleviates TR-mediated repression in vitro. Using stepwise preassembled PICs, the authors show that hTRα targets either the TBP/TFIIA or the TBP/TFIIA/TFIIB steps of PIC assembly for repression. The authors also show that the repression domain of hTRα maps to the C-terminal ligand-binding region and that direct TR-TBP interactions can be inhibited by thyroid hormone. Together, these results suggest a model in which unliganded hTRα contacts promoter-bound TBP and interferes with later steps in the initiation of transcription.

IT **51-24-1**, TRIAC
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**thyroid hormone receptor** α
targeting of TATA-binding protein for transcriptional repression)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

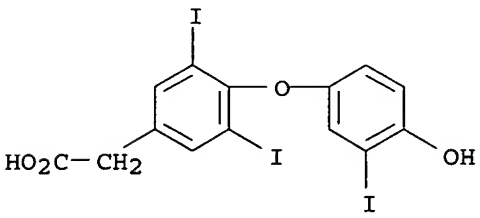


L48 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:556759 HCAPLUS
DOCUMENT NUMBER: 122:282788
TITLE: Ligand modulates the interaction of thyroid hormone receptor β with the basal transcription machinery
AUTHOR(S): Tong, Guo-Xia; Tanen, Michael R.; Bagchi, Milan K.
CORPORATE SOURCE: Population Council, Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Biological Chemistry (**1995**), 270(18), 10601-11
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors investigated the mol. mechanisms underlying the transcriptional silencing and the hormone-induced activation of target genes by thyroid hormone receptor β (TR-β). The authors developed a cell-free transcription system containing HeLa cell nuclear exts. in which unliganded human TR-β represses basal transcription from a promoter bearing thyroid hormone response elements. Binding of hormonal ligand to the receptor reverses this transcriptional silencing. Specific binding of TR-β to the thyroid hormone response element at the target promoter is crucial for silencing. Studies employing TR-β mutants indicate that the silencing activity is located within the C-terminal rather than the N-terminal domain of the receptor. The studies reveal further that unliganded TR-β inhibits the assembly of a functional transcription preinitiation complex (PIC) at the target promoter. The authors postulate that interaction with TR-β impairs the function(s) of one or more assembling transcriptional complexes during the multistep assembly of a PIC. Consistent with this hypothesis, the authors observe that, in the absence of thyroid hormone, TR-β or a heterodimer of TR-β and retinoid-X-receptor undergoes direct protein-protein interactions with the transcription factor IIB-TATA binding protein complex, an early intermediate during PIC assembly. Binding of hormone to TR-β dramatically reduces the interaction between the receptor and the transcription factor IIB-TATA binding protein complex. The authors propose that the role of ligand is to facilitate the assembly of functional PICs at the target promoter by reducing nonproductive interactions between TR-β and the initiation factors.

IT **51-24-1**, TRIAC
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ligand modulation of **thyroid hormone receptor** β interaction with basal transcription machinery)

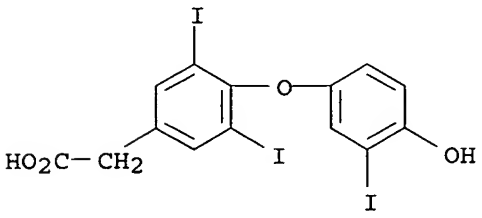
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



L48 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:246037 HCAPLUS
DOCUMENT NUMBER: 122:1504
TITLE: Reconstitution of thyroid hormone receptor and retinoic acid receptor function in the fission yeast Schizosaccharomyces pombe
AUTHOR(S): Sande, Stephen; Privalsky, Martin L.
CORPORATE SOURCE: Department Microbiology, University California, Davis, CA, 95616, USA
SOURCE: Molecular Endocrinology (**1994**), 8(11), 1455-64
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors report here a characterization of the thyroid hormone receptors (T3Rs), retinoic acid receptors (RARs), and retinoid X receptors (RXRs) by reconstituting their actions in the fission yeast Schizosaccharomyces pombe. S. pombe provide a well defined and readily manipulated genetic background devoid of known endogenous nuclear hormone receptors. All the receptors tested, when introduced exogenously into S. pombe, induced high levels of reporter gene activation in response to physiol. concns. of hormone ligand. In these properties, the S. pombe system exhibits significant advantages over the previously employed Saccharomyces cerevisiae system. Use of the S. pombe system permitted the elucidation of previously undescribed differences in the DNA sequence recognition properties of different isoforms of the RXR and RARs, and the identification of apparently novel forms of response element for RXRs and RARs. Intriguingly, the v-erb A allele of T3R, a transcriptional repressor in vertebrate cells, acts as a transcriptional activator both in S. cerevisiae and in the evolutionarily higher divergent S. pombe, underscoring the importance of cellular factors in the regulation of receptor transcriptional activity.

IT **51-24-1**, Triac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**thyroid hormone receptor** and retinoic acid receptor function reconstitution in Schizosaccharomyces pombe)
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

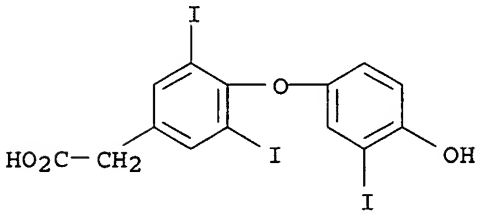


L48 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:596505 HCAPLUS
DOCUMENT NUMBER: 121:196505
TITLE: A chimeric thyroid hormone receptor constitutively bound to DNA requires retinoid X receptor for hormone-dependent transcriptional activation in yeast
AUTHOR(S): Lee, Jae Woon; Moore, David D.; Heyman, Richard A.
CORPORATE SOURCE: Dep. Cell Biology, Ligand Pharmaceuticals Inc., San Diego, CA, 92121, USA
SOURCE: Molecular Endocrinology (**1994**), 8(9), 1245-52
CODEN: MOENEN; ISSN: 0888-8809
DOCUMENT TYPE: Journal
LANGUAGE: English

AB T3 receptors (TRs) regulate transcription by binding to specific DNA response elements as heterodimers with the retinoid X receptors (RXRs). To study the consequences of this heterodimerization for transcriptional regulation in the absence of complications associated with its effects on DNA binding affinity, the authors expressed in the yeast Saccharomyces cerevisiae a chimeric protein consisting of the rat TRβ1 ligand-binding domain fused to the DNA-binding domain of the bacterial repressor lexA (lexATR). LexATR is a weak, T3-responsive activator of a β-galactosidase reporter gene controlled by upstream lexA-binding sites (lexA-β-gal). In contrast, coexpression of human RXRα (hRXRα) strongly enhances both the basal and ligand-induced transcriptional activities. Both the N-terminal activation domain of RXR and sequences at the extreme C terminus of lexATR are required for this T3- and RXR-dependent transcriptional activation. The lexATR chimera was also used to characterize receptor-receptor interactions using the two-hybrid system. Coexpression of B42RXR, a fusion protein of the human RXRα ligand-binding domain and the B42 transcriptional activation domain, strongly increases the transcriptional activity of lexATR in the absence of T3 or 9-cis-retinoic acid. The authors conclude that RXR is essential for full, T3-dependent transcriptional activity of the TR in yeast, and that protein-protein interaction of TR and RXR in vivo is ligand-independent.

IT **51-24-1**, Triac
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chimeric **thyroid hormone receptor** constitutively bound to DNA requires retinoid X receptor for hormone-dependent transcriptional activation in yeast)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

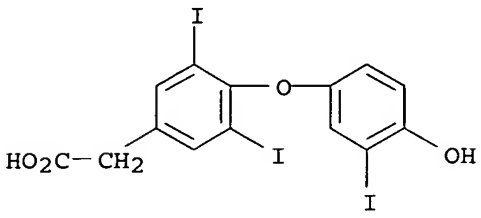


L48 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:662634 HCAPLUS
DOCUMENT NUMBER: 119:262634
TITLE: One-step immunoaffinity purification of human β1 thyroid hormone receptor with DNA and hormone binding activity
AUTHOR(S): Park, Jae Bum; Ashizawa, Kiyoto; Parkison, Clifford; Cheng, Sheue Yann
CORPORATE SOURCE: Lab. Mol. Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Journal of Biochemical and Biophysical Methods (**1993**), 27(2), 95-103
CODEN: JBBMDG; ISSN: 0165-022X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An efficient and versatile method to purify large amts. of active human β1 thyroid hormone receptor (h-TRβ1) was developed. Using a T7 expression system, h-TRβ1 was overexpressed in Escherichia coli. Approx. 80% of the expressed receptor protein was concentrated in the insol. inclusion bodies and .apprx.20% was in the soluble form (h-TRβ1-S). The h-TRβ1-S was conveniently purified by one immunoaffinity chromatog. step. From 1 L of cell culture, approx. 0.1 mg of purified h-TRβ1-S was obtained. The purified h-TRβ1-S binds to 3,3',5-triiodo-L-thyronine with a Ka = 2 + 109 M-1 and exhibits analog specificity. The purified h-TRβ1-S also binds to T3 response elements (TRE) with different orientation in the half-sites with differential activity. In addition, binding of h-TRβ1-S to TREs was enhanced by retinoid X receptor. These results indicate that the purified h-TRβ1-S retains its hormone and DNA binding activity. The purified h-TRβ1-S is suitable for structural and functional studies. This method could be used to purify h-TRβ1 or rat TRβ1 expressed in insect cells or yeast.

IT **51-24-1P**, 3,3',5-Triiodothyroacetic acid
RL: PREP (Preparation)
(β1 **thyroid hormone receptor** binding of, after receptor purification from Escherichia coli by immunoaffinity chromatog.)

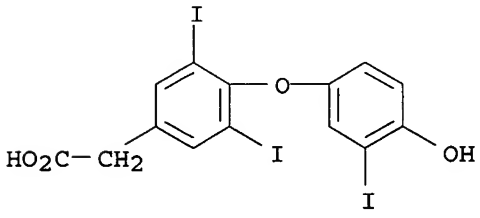
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



L48 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:574528 HCAPLUS
DOCUMENT NUMBER: 119:174528
TITLE: Unliganded thyroid hormone receptor inhibits formation of a functional preinitiation complex: implications for active repression
AUTHOR(S): Fondell, Joseph D.; Roy, Ananda L.; Roeder, Robert G.
CORPORATE SOURCE: Lab. Biochem. Mol. Biol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Genes & Development (**1993**), 7(7B), 1400-10
CODEN: GEDEEP; ISSN: 0890-9369
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The thyroid hormone receptor (TR) belongs to the steroid/nuclear receptor superfamily of ligand-inducible transcription factors. Numerous studies using transient transfection assays have demonstrated that in the absence of thyroid hormone (T3), unliganded TR acts as a constitutive repressor of transcription on genes bearing TR-response elements. The authors examined the mol. mechanism of TR repression in vitro by using both HeLa nuclear exts. and purified basal factors. Unliganded TR was an active transcriptional repressor, distinct from passive repressors that compete with activators for DNA binding. Repression by TR can be relieved by adding the T3 analog triiodothyroacetic acid, suggesting that liganded TR undergoes a conformational change that masks or disrupts the repressor function. Repression by TR is mediated through the basal transcription machinery and can occur independently of previously characterized TATA-binding protein-associated cofactors thought to be involved in either basal repression or activator-dependent transcription. TR inhibits transcription at an early step during preinitiation complex (PIC) assembly, as preassembled PICs are refractory to the inhibitory effects of TR.

IT **51-24-1**
RL: BIOL (Biological study)
(**thyroid hormone receptor**-induced transcription repression reversal by)
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

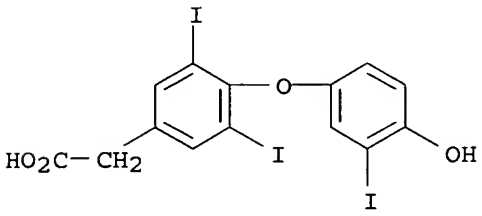


L48 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:33081 HCAPLUS
DOCUMENT NUMBER: 118:33081
TITLE: Conformational changes in chicken thyroid hormone receptor α1 induced by binding to ligand or to DNA
AUTHOR(S): Toney, Jeffrey H.; Wu, Ling; Summerfield, Ann E.; Sanyal, Gautam; Forman, Barry M.; Zhu, Jiabi; Samuels, Herbert H.
CORPORATE SOURCE: Dep. Mol. Pharmacol. Biochem., Merck Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Biochemistry (**1993**), 32(1), 2-6
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A classic model of steroid/thyroid hormone receptor activation postulates that a conformational change or transformation occurs upon ligand binding as a first step toward regulation of gene transcription. In order to test this model, phys. studies have been carried out using purified full-length chicken thyroid hormone receptor α1 (cT3R-α) expressed in Escherichia coli. CD spectroscopic studies reveal that cT3R-α1 adopts a different conformation upon specific binding to a cognate ligand triiodothyroacetic acid as well as to a thyroid hormone response element, an idealized inverted repeat AGGTCA TGACCT. These results suggest that cT3R-α1 may adopt distinct conformations whether free or bound to ligand or to DNA. These states may reflect the changes in the conformation of steroid/thyroid hormone receptors in the signal transduction pathway.

IT **51-24-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**thyroid hormone** α1 **receptor**
binding by, conformational changes in)

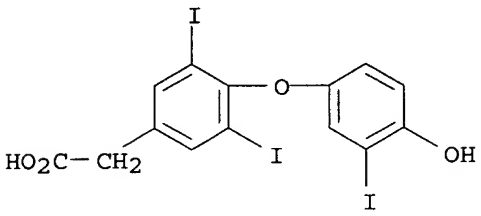
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



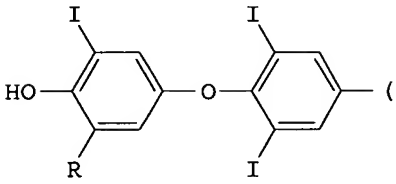
L48 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:504772 HCAPLUS
DOCUMENT NUMBER: 117:104772
TITLE: Thyroid hormone alters in vitro DNA binding of monomers and dimers of thyroid hormone receptors
AUTHOR(S): Ribeiro, Ralff C. J.; Kushner, Peter J.; Apriletti, James W.; West, Brian L.; Baxter, John D.
CORPORATE SOURCE: Metab. Res. Unit, Univ. California, San Francisco, CA, 94143-0540, USA
SOURCE: Molecular Endocrinology (**1992**), 6(7), 1142-52
CODEN: MOENEN; ISSN: 0888-8809
DOCUMENT TYPE: Journal
LANGUAGE: English

AB T3 binds to intranuclear thyroid hormone receptors (TRs) on target DNA elements and exerts profound influences on gene expression by mechanisms not yet characterized. Gel shift assays and crosslinking expts. were used to demonstrate that T3 greatly induced the monomeric binding of the hTRβ produced in E. coli to DNA. T3 also increased the gel mobility of these monomer-DNA complexes suggesting they undergo a ligand-induced conformational change. This effect did not depend on the orientation and spacing of the half-site motifs within the DNA structure. In contrast, T3 had diverse effects on the dimeric interaction. T3 increased the dimeric interaction to the palindrome GGTCA·TGACC (an effect lost by spacing the half-sites with 3 base pairs) and decreased the dimeric interaction to the inverted palindrome containing the TGACC·GGTCA motif. Scatchard analyses indicated that the T3 enhancement on binding was due to an increase in the number of TR with high affinity DNA-binding activity and not by increasing the affinity of TR that could bind to DNA. The effects of various T3 analogs were directly related to their affinities for the TR. These ligand effects on in vitro TR-DNA binding may reflect mechanisms by which T3 regulates transcription in vivo.

IT **51-24-1**
RL: BIOL (Biological study)
(**thyroid hormone receptor** monomer and dimer binding by DNA response to)
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



L48 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:76823 HCAPLUS
DOCUMENT NUMBER: 116:76823
TITLE: α-Methylated analogs of triiodothyroalkanoic acids: synthesis and biological activity
AUTHOR(S): Zenker, N.; Ekpe, A. E.; Hubbard, L. S.
CORPORATE SOURCE: Sch. Pharm., Univ. Maryland, Baltimore, MD, 21201, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(3), 548-52
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

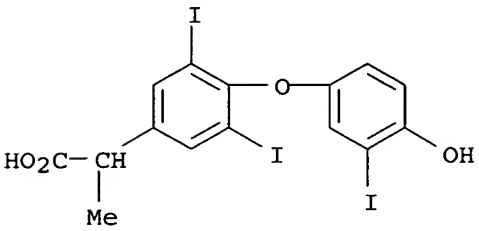


I, R=H, n=0
II, R=H, n=1
III, R=I, n=1

AB Three novel thyroid hormone analogs (I, II, and III) were prepared The hepatic thyroid receptor affinity of these analogs was compared to the other available thyroid analogs. The ability of these compds. to increase the activity of 2 hepatic and to lower blood cholesterol was compared to that of L-triidothyronine. I had less nuclear binding affinity and less enzyme inducing ability, but more blood cholesterol lowering ability than triiodothyroacetic acid. III showed less nuclear binding affinity and less enzyme-inducing activity than II.

IT **186901-85-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and **thyroid hormone receptor** binding and anticholesteremic activities of)

RN 186901-85-9 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo-α-methyl- (9CI) (CA INDEX NAME)

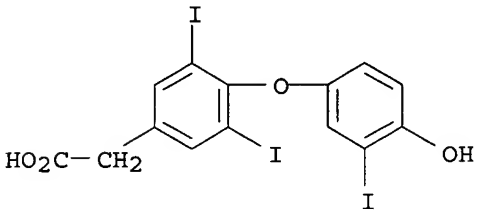


L48 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:34671 HCAPLUS
DOCUMENT NUMBER: 116:34671
TITLE: Functional properties of human thyroid hormone receptor β1 overexpressed using baculovirus
AUTHOR(S): Collingwood, T. N.; Sydenham, M.; Page, M. J.; Chatterjee, V. K. K.
CORPORATE SOURCE: Dep. Med., Univ. Cambridge, Cambridge, CB2 2QQ, UK
SOURCE: FEBS Letters (**1991**), 291(2), 315-18
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have overexpressed the human β1 thyroid hormone receptor in insect cells using a recombinant baculovirus to a level of 5-10% of total cellular protein. The recombinant protein migrates as a 50 kDa band by SDS-PAGE and Western blot anal. The expressed receptor binds to T3 with a Kd of 1.3 + 101-10M and to thyroid hormone analogs with an affinity hierarchy of triiodothyroacetic acid > T3 > T4 > rT3. Gel retardation assays show highly specific receptor binding to a thyroid response element which is modified by the presence of ligand and avidin-biotin complex DNA anal. shows a Kd of 6.2 + 10-10M for this interaction. These results indicate high level expression of human β thyroid hormone receptor with authentic hormone and DNA binding properties.

IT **51-24-1**
RL: ANST (Analytical study)
(recombinant β1 **thyroid hormone receptor** binding with, after overexpression in insect cells)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

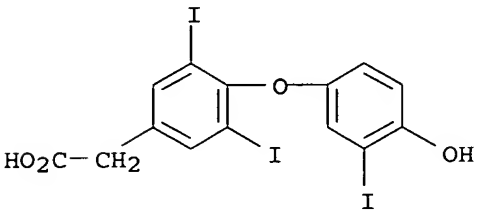


L48 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:179695 HCAPLUS
DOCUMENT NUMBER: 114:179695
TITLE: An adenoviral vector system for functional identification of nuclear receptor ligands
AUTHOR(S): Shih, Wendy; Mears, Tamara; Bradley, David J.; Parandoosh, Zahra; Weinberger, Cary
CORPORATE SOURCE: Ligand Pharm., Inc., San Diego, CA, 92121, USA
SOURCE: Molecular Endocrinology (**1991**), 5(2), 300-9
CODEN: MOENEN; ISSN: 0888-8809
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A recombinant adenovirus system has been designed that confers glucocorticoid responsiveness upon infected cells in culture. Two mutually dependent viruses are required: a trans-activator virus containing the human glucocorticoid receptor transcription unit and a second reporter virus harboring a glucocorticoid response element linked to the firefly luciferase gene. Another reciprocal pair of viruses has been generated; one member expresses the rate thyroid hormone receptor α, while the other contains the luciferase gene regulated by a thyroid hormone-responsive DNA element. Corticosteroid- or thyroid hormone-induced transcription can be efficiently and accurately quantitated from cells coinfected with the appropriate complementary virus pair 20 h after infection in 96-well microtiter plates. This coinfection assay offers a convenient way to measure transcriptional activation by nuclear receptors and has certain key advantages over the commonly used cotransfection method. Its sensitivity and precision make it a practical approach to rapidly identify substances extracted from complex biol. samples activating candidate "orphan" nuclear receptor mols.

IT **51-24-1**, Triac
RL: PRP (Properties)
(transcription activation by **thyroid hormone receptor** α in response to, adenovirus vector system for assay of)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

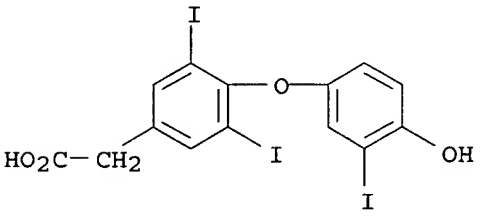


L48 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:401266 HCAPLUS
DOCUMENT NUMBER: 111:1266
TITLE: Trans-activation by thyroid hormone receptors: functional parallels with steroid hormone receptors
AUTHOR(S): Thompson, Catherine C.; Evans, Ronald M.
CORPORATE SOURCE: Howard Hughes Med. Inst., Salk Inst. Biol. Stud., La Jolla, CA, 92138, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1989**), 86(10), 3494-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of thyroid hormones are mediated through nuclear receptor proteins that modulate the transcription of specific genes in target cells. Previously cDNAs encoding 2 different mammalian thyroid hormone receptors were isolated, one from human placenta (hTRβ) and the other from rat brain (rTRα), and their in vitro translation products bind thyroid hormones with the characteristic affinities of the native thyroid hormone receptor. Both of the cloned receptors activate transcription from a thyroid hormone-responsive promoter in a hormone-dependent manner, with rTRα eliciting a greater response than hTRβ. The putative functional domains of the thyroid hormone receptors were examined by creating chimeric thyroid hormone-glucocorticoid receptors, producing receptors with hybrid functional properties. These expts. support the proposal that the thyroid hormone receptors are composed of interchangeable functional domains, and indicate that the mechanism of hormone-inducible gene regulating has been conserved in steroid and thyroid hormone receptors.

IT **51-24-1**, Triac
RL: BIOL (Biological study)
(**thyroid hormone receptor** α- and β-subtypes response to)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

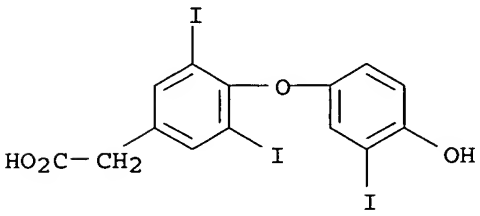


L48 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:180621 HCAPLUS
DOCUMENT NUMBER: 108:180621
TITLE: Characterization of thyroid hormone receptors in human IM-9 lymphocytes
AUTHOR(S): Barlow, John W.; De Nayer, Philippe
CORPORATE SOURCE: Med. Sch., Louvain Univ., Brussels, Belg.
SOURCE: Acta Endocrinologica (**1988**), 117(3), 327-32
CODEN: ACENA7; ISSN: 0001-5598
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In human lymphoblastoid line IM-9 cells, at 37°, nuclear binding of [125I]T3 was saturable (dissociation constant = 34 pmol/L) and of finite capacity (≈350 sites/cell). The binding sites were extracted from a nuclear pellet by treatment with 0.4 mM KCl and sonication. Separation of bound from free [125I]T3 in the exts. was achieved using hydroxyapatite at a concentration of 0.3 mL of a 150 g/L slurry. Rectilinear Scatchard plots were obtained only when the hydroxyapatite was washed with a buffer containing 0.5% Triton X 100. Under these conditions T3 binding sites in the nuclear exts. were present at a concentration of 22.4 fmol/mg protein and showed an affinity of 140 pmol/L at room temperature The same assay system was used to determine the hierarchy of affinities for a range of natural and synthetic analogs. Calling T3 100, the order of potencies observed was: Triac, 500; 3,5-diiodo-3'-isopropylthyronine, 89; T4, 32; 3,5-dimethyl-3'-isopropylthyronine, 2; 3,5-T2, 0.7; rT3, 0.4; 3'5'-T2, <0.01. The T3 binding sites present in human IM-9 lymphocyte nuclei and exts. thereof are evidently thyroid hormone receptors. These cells may be a useful tool to increase understanding of human T3 receptors.

IT **51-24-1**, Triac
RL: PROC (Process)
(**thyroid hormone receptor** binding of, in human lymphocyte)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

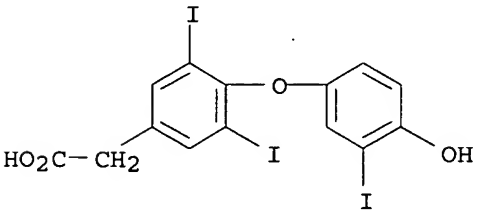


L48 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:69438 HCAPLUS
DOCUMENT NUMBER: 108:69438
TITLE: Existence of nuclear thyroid hormone receptors in the porcine thyroid gland and the rat thyroid cell line FRTL-5
AUTHOR(S): Nakamura, Hirotoshi; Imura, Hiroo
CORPORATE SOURCE: Sch. Med., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Acta Endocrinologica (**1988**), 117(1), 116-24
CODEN: ACENA7; ISSN: 0001-5598
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Whether nuclear T3 receptors exist in the thyroid cell was investigated. Nuclear proteins extracted from porcine thyroid nuclei with 0.4M KCl were incubated with [125I]T3. The mixture was then analyzed by sucrose d. gradient ultracentrifugation which revealed that the T3-binding proteins migrated at the same position of 3.6 S as rat liver nuclear T3 receptors. Fractionation by HPLC using a size exclusion column and an ion exchanger column also demonstrated elution patterns of T3-binding similar to those of the rat liver receptor. Scatchard plots of crude nuclear exts. from porcine thyroid represented a curvilinear pattern. However, when the nuclear proteins partially purified by a DEAE column chromatog. were analyzed, a single binding component was found; the association constant was 4.1 + 1010 L/mol and the maximal binding capacity was 602 fmol T3/mg protein. Displacement study with several T3 analogs showed a highly selective affinity for L-T3. Cultured rat thyroid cells of the FRTL-5 line also contained a single class of saturable, high affinity T3-binding sites. Subconfluent cells in 100-mm dishes were incubated with increasing amts. of [125I]T3 at 37° for 3 h and radioactive T3 in isolated nuclei was counted. Scatchard anal. of data showed that the association constant and the maximal binding capacity were 3.44 + 1010 L/mol and 63.7 fmol T3/mg protein, resp. Apparently, there are nuclear T3 receptors, indistinguishable from the hepatic T3 receptors, in the porcine thyroid and rat FRTL-5 cells.

IT **51-24-1**, Triac
RL: PROC (Process)
(**thyroid hormone receptor** binding of, in thyroid gland and thyroid cell line)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



L48 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:619374 HCAPLUS
DOCUMENT NUMBER: 105:219374
TITLE: Triiodothyronine (T3)-induced down-regulation of the nuclear T3 receptor in mouse preadipocyte cell lines
AUTHOR(S): Pou, Marie Anne; Bismuth, Janine; Gharbi-Chihi, Jouda; Torresani, Janine
CORPORATE SOURCE: Lab. Biochem. Med., Fac. Med., Marseille, 13385/5, Fr.
SOURCE: Endocrinology (**1986**), 119(5), 2360-7
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In preadipocytes cloned from the epididymal fat of lean or genetically obese mice, T3 [6893-02-3] (1.5 nM) decreased the nuclear T3 receptor concentration with no significant change in the affinity for T3. The receptor depletion was time-dependent, rapid, stable in the presence of T3, and reversible in <24 h after its withdrawal. Receptor depletion was also dependent on T3 concentration and close to maximum at 1.5 nM T3; a linear relationship was observed between receptor occupancy by T3 and receptor loss. T4 [51-48-9] and triiodothyroacetic acid [**51-24-1**] also decreased the T3 receptor content, as expected from their affinity for the receptor. Thus, the receptor reduction is evidently related to its occupancy by T3. The reported results, also observed in several other cell types, indicate that down-regulation of the nuclear T3 **receptor** by **thyroid hormones** is probably a generalized event in T3 target cells at least in vitro.

L48 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:619368 HCAPLUS
DOCUMENT NUMBER: 105:219368
TITLE: Identification and characterization of L-triiodothyronine receptors in cells of glial and neuronal origin
AUTHOR(S): Ortiz-Caro, Javier; Yusta, Bernardo; Montiel, Fatima; Villa, Aida; Aranda, Ana; Pascual, Angel
CORPORATE SOURCE: Fac. Med., Univ. Auton. Madrid, Madrid, 28029, Spain
SOURCE: Endocrinology (**1986**), 119(5), 2163-7
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High-affinity, low-capacity binding sites for thyroid hormone were identified in the nuclei of glial (C6) and neuronal (Neuro 2A) cultured cells. Equilibrium dissociation consts., determined by Scatchard anal., were very similar in both types of cells (0.2-0.3 nM). The relative affinity of hormonal analogs was also similar: the affinity for T3 [6893-02-3] was lower than for triiodothyroacetic acid [**51-24-1**] and higher than for T4 [51-48-9] or tetraiodothyroacetic acid [**67-30-1**]. The sedimentation coeffs. obtained by gradient centrifugation of nuclear receptor extracted with 0.4M KCl or excised by micrococcal nuclease digestion were 3.5 S and 6.5 S, resp. Thus, the **thyroid hormone receptor** is not restricted to neuronal cells, but also appears in cells of glial origin.

L48 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:546759 HCAPLUS
DOCUMENT NUMBER: 105:146759
TITLE: Ontogenesis of nuclear T3 receptors in primary cultured astrocytes and neurons
AUTHOR(S): Luo, Min; Faure, Robert; Dussault, Jean H.
CORPORATE SOURCE: Centre Hosp., Univ. Laval, Sainte-Foy, QC, G1V 4G2, Can.
SOURCE: Brain Research (**1986**), 381(2), 275-80
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

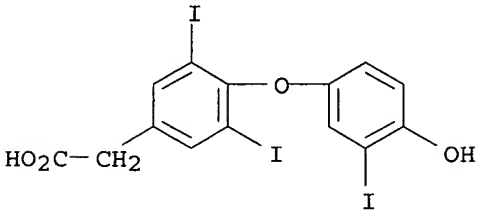
AB Nuclear T3 [6893-02-3] receptor (NTR) were characterized in separated cultures of rat neurons and astrocytes. Scatchard anal. indicated the presence of a single class of high-affinity sites in both cell lines. The apparent equilibrium association constant ranged 1.80 + 1010 - 3.27 + 1010 M-1 in neurons and 1.01 - 1.80 + 1010 M-1 in astrocytes depending on the time in culture. In neurons, the maximal binding capacity (MBC) increased from 0.049 to 0.328 ng T3/mg DNA between 3 and 12 days of culture. In astrocytes, the changes in MBC were less pronounced ranging from a min. of 0.095 ng T3/mg DNA at the 7th day of culture to a maximum of 0.198 ng T3/mg DNA at the 21st day. The relative binding affinity of the **receptor** for **thyroid hormone** analogs was in the order TRIAC [**51-24-1**] > L-T3 > D-T3 [5714-08-9] > L-T4 [51-48-9] in both cell lines. Thus, nuclear T3 receptors similar to those found in vivo are present in primary cultures of both astrocytes and neurons.

L48 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:491787 HCAPLUS
DOCUMENT NUMBER: 105:91787
TITLE: Nuclear thyroid hormone receptors in cultured human fibroblasts: improved method of isolation, partial characterization, and interaction with chromatin
AUTHOR(S): Ichikawa, Kazuo; DeGroot, Leslie J.; Refetoff, Samuel; Horwitz, Allen L.; Pollak, Elizabeth R.
CORPORATE SOURCE: Dep. Med., Univ. Chicago, Chicago, IL, 60637, USA
SOURCE: Metabolism, Clinical and Experimental (**1986**), 35(9), 861-8
CODEN: METAAJ; ISSN: 0026-0495
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to characterize the nuclear **thyroid hormone receptors** in human tissue, an improved method for isolation of nuclei from cultured human fibroblasts provided nuclei with a protein/DNA ratio of 2.8 and a recovery of 42%. The purity of nuclei was verified by phase-contrast and electron microscopy, which showed a normal appearance of chromatin structure. Nuclear binding assay was performed by incubation of whole cells at 37° or isolated nuclei at 22° with L-triiodothyronine (L-T3) [6893-02-3]. In both cases, an affinity constant (Ka) of 2.0-3.0 + 1010M-1 and an average binding capacity of 41 fmol T3/100 μg DNA (3100 binding sites/nucleus) were obtained. During incubation of the nuclei, 13-16% of receptors that had an identical Ka were released into the medium. Salt extraction recovered 85-90% of the receptors, which had a Ka of 4.5 + 1010M-1 and a capacity of 0.13 pmol T3/mg protein. The Ka for L-thyroxine (L-T4) [51-48-9] was 7-18-fold lower than that for L-T3, but the capacity was the same in isolated nuclei, receptors released during incubation of nuclei, and salt-extracted receptors. Of the iodothyronines examined, affinity for triiodothyroacetic acid [**51-24-1**] was the highest, followed by L-T3, D-T3 [5714-08-9], L-T4. Isokinetic glycerol gradient anal. revealed that salt-extracted receptors had a sedimentation coefficient of 3.4 S, whereas micrococcal nuclease digested receptors showed 2 major (6.0-6.5 and 12.5 S) and 2 minor (17 and 19 S) peaks. These results were virtually identical to those obtained with rat liver nuclei analyzed in parallel studies. The nuclear receptors of fibroblasts were more heat labile than those of rat liver, especially at temps. < 40°.

IT **51-24-1**
RL: BIOL (Biological study)
(**thyroid hormone receptor** of human fibroblast affinity for)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

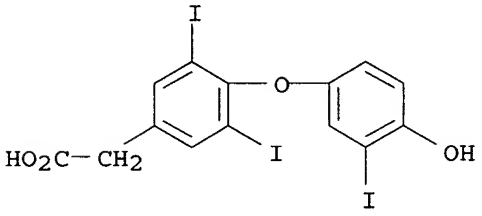


L48 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:401084 HCAPLUS
DOCUMENT NUMBER: 105:1084
TITLE: Use of 125I-triiodothyroacetic acid to measure nuclear thyroid hormone receptor
AUTHOR(S): Evans, R. W.; Braverman, L. E.
CORPORATE SOURCE: Med. Cent., Univ. Massachusetts, Worcester, MA, 01605, USA
SOURCE: Endocrine Research (**1986**), 12(1), 37-47
CODEN: ENRSE8; ISSN: 0743-5800
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 125I-labeled Triac [**51-24-1**] was employed to measure hepatic **thyroid hormone** nuclear **receptor** (RT) in the rat. The binding properties of [125I]Triac and 125I-labeled T3 [6893-02-3] were compared in a 0.4M KCl extract of a liver nuclear preparation The order in which the stable compds., Triac, T3, T4 [51-48-9], and rT3 [5817-39-0] competed for [125I]Triac and [125I]T3 binding in liver nuclear extract was similar (Triac > T3 > T4 > rT3), suggesting association of both radioligands with RT. Scatchard plot anal. of specific [125I]Triac and [125I]T3 binding in nuclear extract gave approx. equal ests. of the maximum binding capacity (MBC). However, the binding affinity, as represented by the equilibrium association constant (Ka), was higher for [125I]Triac than for [125I]T3 (7-10 + 109 M-1 vs. 1-3 + 109 M-1, resp.). To determine the effect of contaminating serum proteins on ests. of MBC and Ka a small amount of dilute rat serum was added to the same nuclear extract preparation Addition of serum decreased the Ka value and markedly increased the MBC values estimated by anal. of [125I]T3 binding data. In contrast, Ka and MBC values derived from [125I]Triac binding data were not influenced appreciably by the addition of serum. These data indicate that: both [125I]Triac and [125I]T3 bound to RT in rat liver nuclear extract; the affinity for RT for [125I]Triac is appreciably greater than for [125I]T3; and ests. of RT concentration (MBC) made with [125I]Triac are less sensitive to serum protein contamination than those made with [125I]T3. These properties of [125I]Triac may be useful in efforts to demonstrate RT in tissues that have low RT levels and(or) when serum contamination is present.

IT **51-24-1**
RL: PROC (Process)
(**thyroid hormone receptor** binding of, in liver nucleus)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

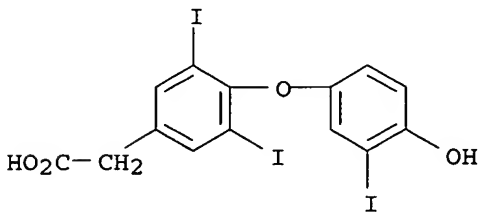


L48 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:1211 HCAPLUS
DOCUMENT NUMBER: 104:1211
TITLE: The early ontogenesis of thyroid hormone receptor in the rat fetus
AUTHOR(S): Perez-Castillo, Ana; Bernal, Juan; Ferreiro, Beatriz; Pans, Teresa
CORPORATE SOURCE: Fac. Med., Univ. Auton. Madrid, Madrid, 28029, Spain
SOURCE: Endocrinology (**1985**), 117(6), 2457-61
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The concentration of **thyroid hormone receptor** binding sites were determined in nuclear exts. derived from rat fetal organs throughout gestation and the postnatal period. Before day 14 of gestation, nuclear exts. were obtained from whole fetuses. No receptor binding activity was detected at day 12 of gestational age, and small amts. were detected at day 13 (maximum binding capacity <50 fmol/mg DNA). The receptor was measured in pools of individual organs from day 14 (brain) or from day 16 (heart, liver, and lung) onwards. The order of analog binding affinity at 14 days was triiodothyroacetic acid [**51-24-1**] = T3 [6893-02-3] > T4 [51-48-9] > rT3 [5817-39-0], suggesting that at 14 days of fetal age the receptor has the same binding specificity as the receptor from mature tissues. In brain, the concentration of binding sites increased from 77 fmol/mg DNA at 14 days to 210 fmol/mg DNA at 17 days, remaining at this level until birth. Receptor concentration was identical whether the binding assays were performed on purified nuclei or nuclear exts. There was no effect of maternofetal hypothyroidism on receptor concentration in the brain at 21 days of gestational age. Lung concns. of receptor also remained constant during the fetal period. During the postnatal period, there was an increase in receptor concentration in brain and lung, with maximum levels at day 6. The pattern of receptor development in heart and liver was different, since its concentration increased progressively throughout the fetal and postnatal periods toward the levels found in adult rat tissues. The appearance of the **thyroid hormone receptor** apparently coincides with that of the first fetal thyroid gland structures, but it occurs much before thyroid function is fully established. As far as the receptor is concerned, fetal tissues have the potential to respond to thyroid hormone as early as the 13th day of gestational age.

IT **51-24-1**
RL: PROC (Process)
(**thyroid hormone receptor** binding of, in fetus)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

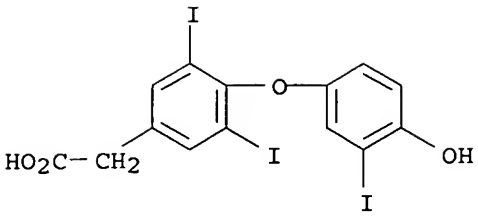


L48 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:607237 HCAPLUS
DOCUMENT NUMBER: 103:207237
TITLE: Studies of nuclear 3,5,3'-triiodothyronine binding in primary cultures of rat brain
AUTHOR(S): Kolodny, J. M.; Leonard, J. L.; Larsen, P. R.; Silva, J. E.
CORPORATE SOURCE: Dep. Med., Brigham and Women's Hosp., Boston, MA, 02115, USA
SOURCE: Endocrinology (**1985**), 117(5), 1848-57
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Primary cultures of enzymically dispersed cells from 17-day-old fetal rat cerebral hemispheres were used to detect the presence of nuclear T3 [6893-02-3] receptors. Cells grown in Min. Essential Medium supplemented with 10% fetal bovine serum were grown in parallel with cytosine-arabinoside (ARA-C)-treated counterparts which were exposed to the antimetabolite for 18 h on culture days 3 and 5 or 4 and 6. Five days after the 2nd ARA-C treatment, phase contrast photomicrographs showed substantial loss of the proliferating basal cells, corresponding to an 85% decrease in cell number Immunocytochem. studies using antiglial fibrillary acidic protein (anti-GFAP) and antineurofilament (anti-NF) antisera demonstrated loss of GFAP-pos. cells (astrocytes) and preservation of NF-pos. cells (neurons), the latter considered to be a nondividing population under the culture conditions. Nuclei obtained from the brain cell cultures at this time by Triton washing bound T3 with properties similar to those observed in vivo. Scatchard anal. showed a single, high-affinity, limited capacity nuclear T3 receptor with a maximal binding capacity (MBC) of 0.53 ng T3/mg DNA and a Kd (dissociation constant) of 0.19 nM.

ARA-C treatment resulted in a mean decrease in DNA per culture dish of 54%, with an accompanying 2-fold enrichment of the MBC and no change in the Kd. In untreated cultures grown for 20 days, DNA per dish increased until day 14 and subsequently remained stable at .apprx.100 μg/dish. The MBC also increased from days 0 to 7, and remained stable until day 14. On day 20, the MBC had declined by .apprx.60% to 0.21 ng T3/mg DNA, at which time the neuron population was decreased. The extracted nuclear receptor from brain cell cultures had a sedimentation coefficient of 3.6S. The relative binding affinities of the nuclear receptor for T3 and several analogs were identical to those found in vivo, making significant contamination of the nuclei with cytosolic or serum binding proteins very unlikely. Nuclei isolated from long term, neuron-free glial cell cultures failed to show any consistent high-affinity saturable T3 binding. Evidently, primary brain cell cultures of dispersed fetal rat cerebral hemispheres contain nuclear T3 receptors similar in quantity, affinity, and specificity to those found in vivo. The ARA-C-susceptible dividing cells in these cultures apparently lack detectable nuclear T3 receptors and appear to be of glial origin. Most, if not all, nuclear T3 receptors are in neurons, and the number of receptors per neuronal nucleus may increase over the 1st week in culture, approaching the quantity seen in the pituitary.

IT **51-24-1**
RL: PROC (Process)
(**thyroid hormone receptor** binding of, in brain nucleus of embryo in culture)
RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)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L48 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:466563 HCAPLUS
DOCUMENT NUMBER: 101:66563
TITLE: Characterization of thyroid hormone stimulation of uridine uptake by rat pituitary tumor cells
AUTHOR(S): Halpern, Jane; Hinkle, Patricia M.
CORPORATE SOURCE: Cancer Cent., Univ. Rochester, Rochester, NY, 14642, USA
SOURCE: Endocrinology (**1984**), 115(1), 95-101
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

AB T3 [6893-02-3] caused a dose-related increase in the rate of [3H]uridine uptake into GH4C1 rat pituitary tumor cells. T3 increased uridine uptake to 130-180% of the control value, with a half-maximal effect at .apprx.1 nM and exerted a half-maximal effect at 1 h and a maximal effect at 2 h. Epidermal growth factor [62229-50-9] also increased uridine uptake by 75%, with an ED50 of 0.6 ng/mL (0.1 nM), but a half-maximal response required 4 min and a maximal effect required 20 min. T3 increased the rate of uptake at all uridine concns. from 30 nM to 130 μM. Equilibrium binding of [125I]T3 to nuclear receptors required from 15 min at 50 nM [125I]T3 to 1 h at 0.5 nM, indicating that occupancy of nuclear receptors precedes maximal stimulation of uridine uptake. T3 did not stimulate the rate of uridine uptake at 20°, when binding to nuclear receptor does not occur. Various thyroid hormones caused an increase in uridine uptake, with the rank order of potency 3,3',5-triiodothyroacetic acid [**51-24-1**] > T3 > L-T4 [51-48-9] > D-T4 [51-49-0] .simeq. 3,3',5,5'-tetraiodothyroacetic acid [**67-30-1**]; rT3 was inactive. This order parallels the affinities of these compds. for nuclear **thyroid hormone receptors.**

L48 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1982:520914 HCAPLUS
DOCUMENT NUMBER: 97:120914
TITLE: Nuclear 3,5,3'-triiodothyronine receptors in rabbit lung: characterization and developmental changes
AUTHOR(S): Gonzales, Linda W.; Ballard, Philip L.
CORPORATE SOURCE: Cardiovasc. Res. Inst., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Endocrinology (**1982**), 111(2), 542-52
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English
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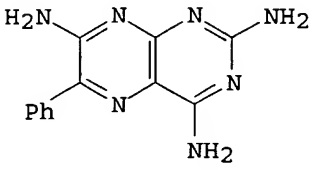
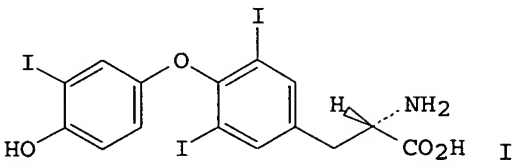


I

AB The T3 (I) [6893-02-3] binding properties of lung nuclei from fetal and adult rabbits were characterized. The developmental profile of nuclear binding capacity was multiphasic. The concentration of sites increased from 0.267 fmol T3 bound/μg DNA at 21 days of gestation to 0.384 fmol/μg DNA at 28 days of gestation and then decreased to 0.273 fmol/μg DNA by term. Within 2-3 wk after birth, the concentration rose to 0.321 fmol/μg DNA before decreasing to the adult concn (0.238 fmol/μg DNA). Maximal T3 binding to lung nuclei was achieved after incubation of fetal nuclei for 90 min at 37° and adult nuclei for 4 h at 25°. The half-times of T3 dissociation from fetal nuclei were 28 min at 37°, 2.5 h at 30°, and 24-36 h at 2°; the dissociation rates for adult nuclei were similar. The relative order of potency of T3 analogs for both fetal and adult nuclei was T3 propionate [51-26-3] > 3,3',5-triiodothyroacetic acid [**51-24-1**] > L-T3 > D-T3 [5714-08-9] > L-T4 [51-48-9] > 3,5-diethyl-3'-isopropyl-D]-thyronine [82911-14-6] > rT3 [5817-39-0] > 3,5-dimethyl-3'-isopropyl-L-thyronine [26384-44-1]. The release of receptors from nuclei incubated under optimal conditions was similar for fetal and adult nuclei (9.8 and 10.2%, resp.). Receptor release was independent of gestational age and T3 and Ca2+ concns., but was dependent on incubation temperature and time. Nuclear receptors from adult, but not fetal, lung were inactivated during incubation at 37° and were protected by the presence of a saturating T3 concentration, suggesting the greater stability of occupied than unoccupied receptors. A procedure for estimating the occupancy of fetal **receptors** by endogenous **thyroid hormone** is described. This assay is based on the lower T3 binding to nuclei at 2° than at 37°, and was validated by altering the nuclear T3 content both in vitro and in vivo. Occupancy of receptors increased from .apprx.11 to 23% of the total binding capacity between 21 and 28 days of gestation. Thus, the nuclear T3 receptors in rabbit lungs undergo changes in concentration, stability, and occupancy during pre- and postnatal life. Both endogenous and exogenous thyroid hormones apparently have a direct action in fetal lung maturation.

L48 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:631319 HCAPLUS
DOCUMENT NUMBER: 93:231319
TITLE: Molecular interactions between thyroid hormone analogs and the rat liver nuclear receptor. Partitioning of equilibrium binding free energy changes into substituent group interactions
AUTHOR(S): Bolger, Michael B.; Jorgensen, Eugene J.
CORPORATE SOURCE: Dep. Pharm. Chem., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Journal of Biological Chemistry (**1980**), 255(21), 10271-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

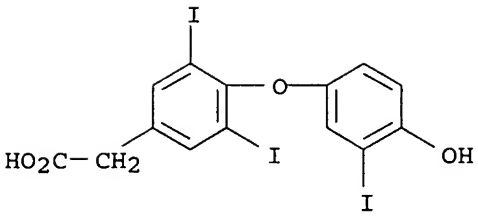


I

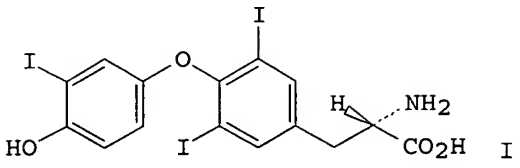
AB The binding affinities of 125I-labeled L-3,5-triiodothyronine (I) [6893-02-3] and a series of thyroid hormone analogs to the solubilized rat liver nuclear receptor provided information about the structural and stereochem. nature and magnitude of interactions in the hormone-receptor complex. The receptor binding affinities of 57 thyroid hormone analogs were determined in a competitive binding assay with I-125I (Ka = 1.2 + 109M-1). These results were used to calculate the free energy of binding (ΔG°) for each analog in order to determine, by 1st order partitioning of free energies, the nature and magnitude of specific substituent interactions with the receptor. The binding of I-125I to the solubilized receptor is associated with a change in free energy, ΔG° = -12.4 kcal/mol. The 4'-hydroxy participates in a donor hydrogen bond oriented toward the 5' side of the outer ring and adds -1.2 kcal/mol of binding free energy. The 3'-substituent participates in direct hydrophobic and van der Waals bonding with a size limit at iso-Pr. The 3'-substituent also enhances the strength of the 4'-hydroxy interaction. The contribution to the binding free energy of a 3'-iodine in I is -4.1 kcal/mol. The optimal 3,5-substituents are iodine atoms which can each contribute an average of -3.4 kcal/mol. This value contains the interactive effect on orientation of the outer ring, as well as the direct contribution to binding by the 3,5-iodine atoms and the aromatic rings. The alanine side chain probably participates in an electrostatic attraction between the carboxylate anion and a pos. charged amino acid residue in the receptor but due to the presence of the α-ammonio group adds a negligible -0.2 kcal/mol.

IT **51-24-1**
RL: PROC (Process)
(**thyroid hormone receptor** binding of, in liver nuclei, structure in relation to)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)


I
O
HO2C— CH2
I
OH
I

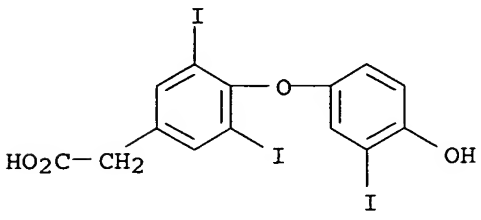
L48 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:191633 HCAPLUS
DOCUMENT NUMBER: 92:191633
TITLE: Evidence of specific nuclear binding sites for T3 in the mouse cultured fibroblast
AUTHOR(S): Brisson-Lougarre, A.; Jozan, S.; Blum, C.
CORPORATE SOURCE: Lab. Endocrinol. Exp., Cent. Hosp. Univ. Rangueil, Toulouse, Fr.
SOURCE: Journal of Endocrinological Investigation (**1979**), 2(4), 437-40
CODEN: JEIND7; ISSN: 0391-4097
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



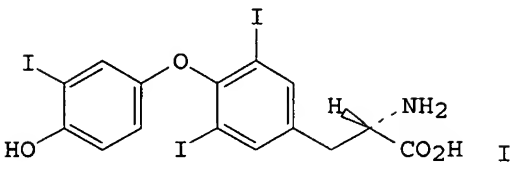
AB An L-triiodothyronine (L-T3)(I) [6893-02-3]-specific receptor was identified in the nuclei of cultured fibroblasts by means of labeling with triiodothyronine-125I. These receptors, which were present at a concentration of 2000 sites per nucleus, were saturable and of a high binding affinity. Displacement of triiodothyronine from the receptors by thyroid hormone analogs generally correlated with the thyromimetic potency of the analogs.

IT **51-24-1**
RL: PROC (Process)
(**thyroid hormone receptor** binding of, in cell nucleus of fibroblast)

RN 51-24-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3-iodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)

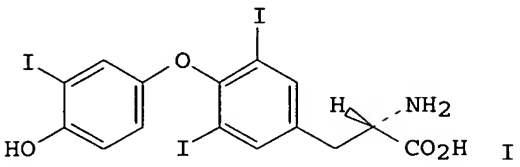


L48 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:115512 HCAPLUS
DOCUMENT NUMBER: 90:115512
TITLE: Nuclear thyroid hormone receptors in a human breast cancer cell line
AUTHOR(S): Burke, Robert E.; McGuire, William L.
CORPORATE SOURCE: Dep. Med., Univ. Texas Health Sci. Cent., San Antonio, TX, USA
SOURCE: Cancer Research (**1978**), 38(11, Pt. 1), 3769-73
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Proliferation of a human metastatic breast cancer cell line (MCF-7) was stimulated by the addition of 3,3',5-triiodothyronine (I) [6893-02-3] to the culture medium. An optimal effect was observed near 5 + 10-10M. **Thyroid hormone receptor** was assayed by comparing the radioactive I [125I] incorporated by MCF-7 cells incubated in culture with and without unlabeled competitor. Bound I[125I] in the nuclei was determined directly by counting Triton X-100-purified nuclear pellets. Saturable or competible binding was not demonstrable for whole cells. MCF-7 nuclei contained a relatively small number of specific I binding sites (20 fmol/100 μg DNA, or 1200 sites/cell) with high affinity (Kd = 1 + 10-10M). The relative effectiveness of unlabeled structural analogs to I as competitors for I[125I] binding was I = 3,5-diiodo-3'-isopropyl- L-thyronine [51-23-0] > D-3,3'-5-triiodothyronine [5714-08-9] > D-thyroxine [51-49-0] = 3,3',5,5'-tetraiodo-L-thyroacetic acid [**67-30-1**] > 3,3'5'-triiodo-L-thyronine [5817-39-0]. Nuclear receptor levels were not altered by treatment of MCF-7 cells with these compds. or with I itself. Receptor levels also did not fluctuate with the growth phase. Apparently, **receptors** for **thyroid hormone** are present in nuclei of cells derived from a human breast cancer.

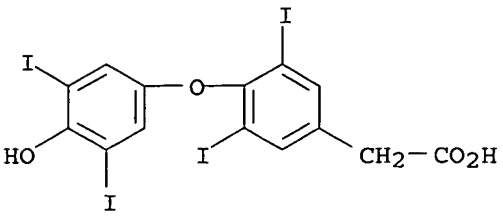
L48 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:417270 HCAPLUS
DOCUMENT NUMBER: 89:17270
TITLE: The mitochondria as a site of thyroid hormone action
AUTHOR(S): Sterling, Kenneth; Milch, Peter O.
CORPORATE SOURCE: Dep. Med., Columbia Univ. Coll. Physicians Surg., New York, NY, USA
SOURCE: International Congress Series (**1976**), 378(Thyroid Res.), 342-6
CODEN: EXMDA4; ISSN: 0531-5131
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The association consts. of an isolated liver mitochondrial membrane protein for 3,3',5-triiodothyronine (I) [6893-02-3], thyroxine [51-48-9], tetraiodothyroacetic acid [67-30-1], D-thyroxine [51-49-0], and 3'-isopropyl-3,5-diiodo-D-thyronine [51-23-0] were .apprx.3 + 1011, 1 + 1011, 3 + 109, 1 + 1010, and 2 + 1012 L/mol. resp. Similar values were found for a kidney mitochondrial membrane protein. The association consts. for I binding in the liver cytosol and nuclei were .apprx.2 + 106 and 5 + 1/8 L/mol, resp. Thus, the mitochondria may contain a high affinity specific binding protein for thyroid hormones.

IT **67-30-1**
RL: PROC (Process)
(mitochondria binding of, **thyroid hormone receptor** in relation to)

RN 67-30-1 HCAPLUS
CN Benzeneacetic acid, 4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodo- (9CI) (CA INDEX NAME)



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